CANCER CARE

Searching for balance

DIAGNOSIS

ASSESSMENT

[illegible]

[illegible]

The Ontario Cancer Treatment and Research Foundation was incorporated in 1943 by an Act of the Legislature of the Province of Ontario and reconstituted by The Cancer Act, 1957. The Cancer Act states that, "The object of the Foundation is to establish and conduct a program of research, diagnosis and treatment in cancer, including,

(a) the establishment, maintenance and operation of research, diagnostic and treatment centres in general hospitals or elsewhere;

(b) the transportation of patients and escorts to its treatment centres or to the hospital of the Institute for diagnosis, treatment or investigation;

(c) the establishment, maintenance and operation of hostels in connection with its treatment centres or the hospital of the Institute;

(d) the laboratory and clinical investigation of cancer problems;

(e) the co-ordination of facilities for treatment;

(f) the adequate reporting of cases and the recording and compilation of data;

(g) the education of the public in the importance of early recognition and treatment;

(h) the providing of facilities for undergraduate and postgraduate study;

(i) the training to technical personnel; and

(j) the providing and awarding of research fellowships."

Part II of The Cancer Act, dealing with The Ontario Cancer Institute, as amended by The Cancer Amendment Act, 1968-69, provides that the Institute Board shall consist of 15 persons appointed by the Lieutenant Governor in Council. Five members of the Institute Board shall be representatives of the Foundation, one of whom shall be the chairman of the Foundation. The Act specifies that one of the Foundation representatives on the Board of the Institute shall be the chairman of the Institute.

COVER DESIGN BY:
OHA Creative Services

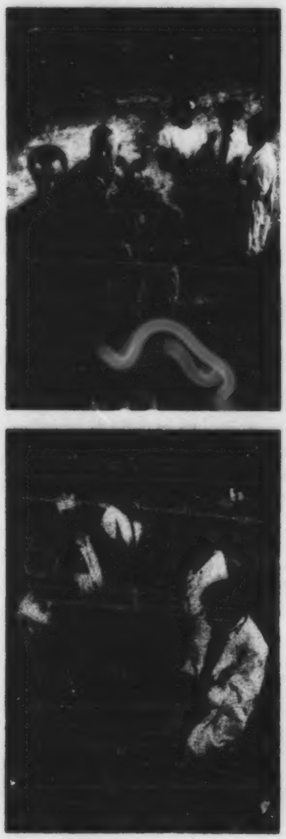
Printed in Canada
ISSN 0315 - 9884

CANCER IN ONTARIO 1990

92-03629/

CANCER CARE

Searching for balance



The Cover

The secret of care is caring for the patient. Modern technology, which has increased the number and range of treatments for cancer, demands more of the treatment team's time, energy and attention. Our cover illustrates the search for balance between the process of diagnosis, assessment and specific treatment, and the care of the patient as a person. This balance, when struck, will empower the individual to participate in his/her care and will contribute to healing and/or adaptation to the disease.

GUEST EDITORS:
A. David Ginsburg
Jack C. Laidlaw

EDITOR:
John O. Godden

ASSISTANT EDITOR:
Krystyna Kwiatkowska

OCTRF

The Ontario Cancer Treatment and Research Foundation

**7 Overlea Boulevard, Toronto,
Ontario, Canada, M4H 1A8**

CONTENTS

Message from the Chairman 1

President's Report 3

Obituaries 5

CANCER CARE: SEARCHING FOR BALANCE – A SYMPOSIUM

Foreward 11

The Experience of Cancer 12

Facing Cancer
R. Sheppard 14

Face to Face: The Rabine-Clarke Dialogue
E.A. Clarke 19

Physicians and the Dying: Searching for the Human Connection
E. Seravalli and J. Fashing 27

Psychosocial Oncology — An Overview
A.D. Ginsburg 30

Needs of Cancer Patients in Ontario
J. Loveridge and M. Istiloglu 39

Cancer 2000: Building a United Community
Wm.K. Adair and M.I. Fitch 46

Inequalities in Cancer Control in Canada
J.C. Laidlaw 51

Research and Clinical Decision Making and Health-Related Behaviour
J.E. Till and H.J. Sutherland 53

Behavioural Research and Cancer
P.G. Scholefield 57

Helping Patients Cope with and Combat Cancer
A.J. Cunningham 61

Pallitative Care and the Control of Suffering
J.F. Scott 63

Meaning of Pain in Cancer
C. Davis 69

Patient Care Delivery Systems: "Supportive Care" in Practice
L.S. Thomson 74

Enhancing the Quality of Life of the Cancer Patient and the Oncologist: Referral to the Psychologist — Who and When?
R.A.A. Buckman and B.D. Doan 78

Stress and Coping in Cancer Professionals
M.L.S. Vachon 87

The Place of Social Work in Psychosocial Oncology
A. Sawarna 93

A Community Cancer Outreach Program
S. Markland 98

Research and Coping Interventions
S. Sellick 104

Psychosocial and Pallitative Care at the Hamilton Regional Cancer Centre 109

Supportive Care Initiatives at the Kingson Regional Cancer Centre .. 112

Department of Psychosocial Services at the Thunder Bay Regional Cancer Centre 113

Psychosocial and Pallitative Care for Patients with Cancer at the Windsor Regional Cancer Centre 115

EDUCATION

Summary of OCTRF Education Activites 119

12th Clinical Cancer Research Conference 122

Summary of the 26th OCTRF Clinical Conference: Lung Cancer in the 1990s 124

REGIONAL CANCER CENTRES

OCTRF Regional Cancer Centres 129
- Hamilton Centre 131
- Kingston Centre 135
- London Centre 138
- Northeastern Ontario Centre 143
- Ottawa Centre 146
- Thunder Bay Centre 154
- Toronto-Bayview Centre 157
- Windsor Centre 160

Service Load 163

Consultative and Follow-up Clinics by Zones of Service 169

Clinical Consultants at OCTRF Regional Cancer Centres and the Princess Margaret Hospital 171

THE ONTARIO CANCER INSTITUTE

The Ontario Cancer Institute Incorporating the Princess Margaret Hospital 179

SPECIAL SERVICES

Provision of Drugs to Treat Malignant Disease 187

Carcinoembryonic Antigen (CEA) and Steroid-Receptor Assays 188

Diagnostic Biopsy Service and Voluntary Reporting by Pathologists .. 190

Lodges for Ambulatory Cancer Patients 190

Transportation of Cancer Patients 191

Cancer Information Service 191

Ontario Breast Screening Program 192

RESEARCH PROGRAMS

Summary of OCTRF Research 197

Research Personnel Supported by the OCTRF 200

Reports on Research Projects by City, Institution, Title and Author .. 201

EPIDEMIOLOGY AND STATISTICS

Division of Epidemiology and Statistics 289

Cancer Incidence, Mortality and Treatment in Ontario 292

DIRECTORY

Members of the Ontario Cancer Treatment and Research Foundation and its Committees 315

Foundation Corporate Office Staff 320

APPENDICES

Appendix A: Bequests and Donations 323

Appendix B: List of Articles Published in 1989 by Research Personnel, Members of the OCTRF Staffs at the Regional Cancer Centres and Head Office and the Staff of the OCI/PMH 326

MESSAGE FROM THE CHAIRMAN

Photo: Tony V. Hauser

During 1990 the number of "core" cancer cases referred to the Foundation's eight regional centres increased by an estimated 14%! This "core" case increase excludes benign, paraneoplastic and non-melanotic skin cancers and consists of patients, who require high-intensity diagnostic and treatment interventions. As a result, strains have been placed on space, radiotherapy machines, staff and funding.

We have developed a capital (space and major equipment) forecast for the 90s and are working with Government on its implementation. During the year, Government announced a change in funding policy to provide up to 100% of capital costs for new or enhanced facilities planned for or in progress for our Centres in Hamilton, Kingston, Ottawa (Civic and General Divisions), Sudbury, Thunder Bay, Toronto (Bayview) and Windsor. In addition, the Ministry announced three new cancer centres for Metropolitan Toronto during the decade and we are in the process of planning for the first of these.

A mini-expansion of our Toronto-Bayview Centre, which opened on September 18, 1990, provides additional radiotherapy facilities. We are grateful to the City of North York, which funded one-third of the cost; the remainder was provided by Government. Also completed was a new research facility, a co-operative venture of the Foundation, The Sunnybrook Health Science Centre and the University of Toronto.

The new Northeastern Ontario Regional Cancer Centre, which is affiliated with the Laurentian Hospital in Sudbury, began treating patients with radiotherapy on November 5, 1990.

We continue to interact with the Government at a Board level through regular meetings of a Joint Ontario Cancer Treatment and Research Foundation/Ministry of Health Liaison Committee.

In closing, once again may I thank, through their Government, the people of Ontario, the Canadian Cancer Society Ontario Division, the staff of the Regional Cancer Centres and Head Office, OCI/PMH, host hospital and medical schools for their continued support, which has made our programs of patient care, research and education, meaningful realities.

Michael A. Meighen, Q.C.
Chairman

PRESIDENT'S REPORT

1990 was an active year with much planning and many changes in programs, facilities, and organization driven in large part by new initiatives and a continued growth in patient volumes.

The Ontario Breast Screening Program was launched by the opening of two screening centres in London and Scarborough. An additional eight are planned in 1991.

The demand for prompt access to radiotherapy has made it necessary to reactivate mechanisms to refer patients from centres with long waiting lists to centres with some spare capacity. Planning for and completion of the new facilities described by the Chairman will alleviate these difficulties in part. In addition, we are planning to educate the increased numbers of professional staff needed to cope with a significant increase in patient load.

We are continuing to plan for patient care in the future. Important areas of consideration include our linkage with the community, the means of more effective prevention, and modern programs in psychosocial and palliative care. These last aspects are the subject of a series of essays elsewhere, in this report.

Our future research also will consider how we can contribute in such new areas as prevention, behaviour, quality of life and health-care delivery.

As in many areas of health care, there are never enough dollars to do everything everyone wants. In all our planning we endeavor to examine critically our priorities so as to maximize cost effectiveness. To this end, I welcome Mr. Harold Wodinsky, who has joined us as Executive Vice-President and Chief Operating Officer.

During 1990, to strengthen the strategic planning process, we have appointed Ms. Molly Fuchs as Director, Strategic and Operational Planning. Also we have appointed Mr. Michael Muller as Director of Facilities Planning and Development to oversee and co-ordinate the Foundation's capital planning function.

Because the foundation works with many people in diverse constituencies we need to strive constantly for improved communication and understanding. To assist in this area, Ms. Deborah Blackstone will join the Foundation in February 1991 as Director of Communications and Public Affairs.

In the Regional Cancer Centres we have strengthened the administrative structure by appointing chief operating officers. May I welcome them all.

We have appointed professional advisory committees in radiation and medical oncology, medical physics, radiation technology and nursing to help us plan for improved patient care, education and research.

Continuing with its mandate to establish a comprehensive human resource program, the Department of Human Resources has completed a number of key projects. Of particular note, the Department designed and implemented a policies and procedures manual, arranged employee and spousal pension seminars, and supervised recruitment training for managers. In addition, the Department negotiated six labor contracts and met the final requirements of the French Language Services Act. Progress continues in pay equity and job evaluation, and in the fourth quarter the Department established a recruitment function.

During the year Information Systems made a great deal of progress toward the introduction of a new patient management system, the development of a prototype system to support breast screening and enhancement of systems to support the Ontario Cancer Registry.

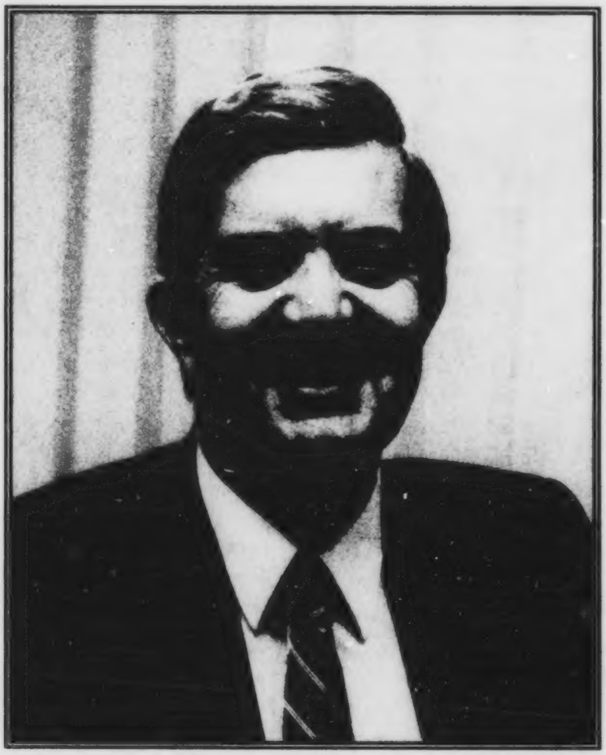
It is with regret that I record the deaths during the year of several esteemed colleagues: Drs. Raymond S. Bush, Dugald H. Thomson, William E. Rawls and recently W.D. (Bill) Rider. They all contributed significantly to cancer control in Ontario and will be sorely missed.

It was a pleasure to meet many of you at the 12th OCTRF Clinical Research Conference at Geneva Park, Lake Couchiching in April 1990, organized by the Ottawa Regional Cancer Centre, and the 26th OCTRF Clinical Conference in Sudbury in November 1990, organized by the Northeastern Ontario Regional Cancer Centre.

In closing I wish to thank the Board, the staff of the Regional Cancer Centres and the Head Office for their support in these challenging times. Finally I wish to acknowledge support of the Foundation's work by the Government of Ontario, the Canadian Cancer Society Ontario Division, and the many patients, their families and friends without whose help we could not complete our tasks.

J. William Meakin, M.D., FRCPC
President and Chief Executive Officer

OBITUARIES



Dr. Raymond S. Bush
1931-1990

On June 29, 1990, at the age of 59, Dr. Raymond Bush, past Director of the Princess Margaret Hospital and Ontario Cancer Institute, died of lung cancer. At the time of his death he was a Professor of Radiology and Associate Professor of Medical Biophysics at the University of Toronto and a member of the Department of Radiation Oncology of the Princess Margaret Hospital (PMH) in Toronto.

Dr. Bush was born on April 11, 1931, in Toronto but was raised in England. He obtained a Bachelor of Science in Physics from the University of London in 1951. Then he returned to Canada and worked as a physicist for Atomic Energy of Canada in Ottawa. In 1956, he entered the medical school at the University of Toronto from which he graduated in 1961, having taken a year off to work as a physicist at the cancer clinic in Rangoon, Burma. In 1962, he entered the radiation oncology residency program at the PMH and completed his qualifying exams in 1965. During this time, he was involved in radiation biology research under the direction of Dr. Robert Bruce in the department of Medical Biophysics, obtaining a Master's degree in 1964. In 1965-66 he was a Gordon Richards Fellow at the Christie Hospital in Manchester, England and, on his return to Canada in 1966, he joined the Department of Radiation Oncology at the PMH.

While pursuing a full-time radiation oncology practice and initiating studies in the management of ovarian cancer, Dr. Bush continued research on the effects of hypoxia on the radiation sensitivity of tumors. His clinical and laboratory studies of the effects of anemia and transfusion provided evidence that hypoxia is an important factor in the control of cancer of the cervix by radiation. These studies led to further laboratory work on fractionation effects and early studies with hypoxic cell sensitizers, both experimental and clinical. In clinical research, his publications on the role of radiotherapy in the management of malignant lymphoma remain a guide for clinicians to the present day. However, his main clinical interest was gynecological malignancy; his work on the role of abdominopelvic radiation in ovarian cancer is recognized internationally. In 1979, his book Malignancies of the Ovary, Uterus and Cervix embodied his philosophy for the optimal treatment of these diseases.

In 1976, at the age of 46, Dr. Bush became the Director of the Ontario Cancer Institute/Princess Margaret Hospital (OCI/PMH). In spite of demanding administrative commitments, he continued his active involvement in clinical research and practice. His vision of the OCI/PMH was that of a centre of excellence in research as well as in the clinical care of the individual patient. In large part his influence was responsible for the shaping of a distinct PMH philosophy of clinical research and practice. His influence on others as a colleague and teacher will continue to be felt for years to come.

During his term as Director of OCI/PMH, Dr. Bush strove to convince the health authorities of the need for expanded and improved facilities for the treatment and care of cancer patients in Ontario. These efforts culminated in 1986 with a commitment by the Ontario Provincial Government to rebuild and expand PMH/OCI. Now planning for this new facility is in its final stages.

Two years ago Dr. Bush stepped down as the Director of the OCI/PMH to return to the full-time academic practice of radiation oncology. He had great plans for the future but his untimely death foreshortened what would have undoubtedly been a further productive period. To the last day of his life, he remained interested in the development of the Institute.

Among Dr. Bush's contributions to oncology was long service to the National Cancer Institute of Canada as a member of the Board of Directors and as President from 1980 to 1982. He served on numerous oncology task forces at the provincial, national and international levels. He was recognized as a world leader in radiation oncology and, in 1989, was elected President of the International Society of Radiation Oncology. Dr. Bush was the recipient of many honors and medals. Among these were a gold medal from the Gilbert H. Fletcher Society and the Franz Buschke, Finzi Memorial and Elis Berven lectureships. As a visiting professor, he travelled all over the world sharing his knowledge and his philosophy of cancer treatment. His talks were known for their diversity and originality. He helped to establish radiation oncology as a distinct clinical specialty.

Dr. Bush led an active and varied life outside OCI/PMH. In his youth he was an outstanding soccer player and in his later years he carried this interest in sports into other areas. Many colleagues and friends will remember his infectious enthusiasm and competitive spirit during games of curling and golf. He was a keen photographer and a good artist, although he had little time to pursue these interests.

In 1959 he married his wife Margaret and, with her, raised three daughters: Catherine, who is a writer; Elizabeth, who recently completed a Master's degree in Botany; and Jennifer, who is working in Africa with the United Nations Development Program. Dr. Bush is also survived by his parents and a sister. We extend our deepest sympathy to the whole family. He will be greatly missed by his colleagues, his patients, his friends and the radiation oncology community to which he contributed so much.

Drs. M. Gospodarowicz and R.P. Hill

Dr. Dugald Hunter Thomson
1924-1990

The London Regional Cancer Centre was saddened by the death of Dr. Doug Thomson on September 18, 1990, in London. Dr. Thomson practised radiation oncology at the London Centre from 1953 to 1981.

Dr. Thomson was born in Glasgow, Scotland. He graduated from Glasgow University Medical School in 1947 and did postgraduate training in radiation oncology in Glasgow, receiving the D.M.R.T. in 1952. He emigrated to Canada in 1953 and took a position as therapeutic radiologist at the London Clinic. He also was appointed Lecturer in the Department of Radiology at the University of Western Ontario. In 1960, with the formation of the Department of Therapeutic Radiology, Dr. Thomson was appointed Clinical Assistant Professor and, in 1972, Clinical Professor. In 1963, he was appointed Senior Therapeutic Radiologist in London, a position he held until 1980.

During his 27 years in London and with the OCTRF, Dr. Thomson served on a number of committees and sub-committees, demonstrating throughout a practical approach to problem-solving. He had a particular interest in medical records and in the operation of tumor registry and was an acknowledged expert in this field. In the early 1950s, Dr. Thomson participated in the first delivery of supervoltage irradiation in London and co-authored the first book published on cobalt-60. He established a reputation as a compassionate, caring physician and was exemplary role model for his peers and students.

In 1980, Dr. Thomson left London to become the first Director of the Cancer Treatment and Research Foundation of Nova Scotia and the first Professor of Radiation Oncology at Dalhousie University in Halifax. He retired in 1989 and returned to London. Dr. Thomson's wife, Nan, passed away in London on October 19, 1990. Dr. and Mrs. Thomson are survived by three sons and one daughter.

CANCER CARE

SEARCHING FOR BALANCE

A SYMPOSIUM

FOREWORD

Cancer treatment is focused predominantly on surgery, radiotherapy and chemotherapy; and, in turn, cancer research is focused predominantly on etiology and treatment. As a consequence, there has been considerable improvement in the control of these diseases, with prolongation of life in many, and even cure in some patients with some cancers.

However, even those who are cured may continue to live under the Sword of Damocles; and, for the majority, cancer is a chronic illness that often is associated with the fear of pain, loss of control and disfigurement, and the everpresent spectre of death and the loss of a loved one. Whether because of the nature of the illness itself or the atmosphere of fear which it evokes, cancer poses special problems. Therefore we MUST be concerned not only with the provision of optimum technical care, but also with the provision of optimum supportive care in a sensitive and caring fashion which will preserve and even enhance the quality of life of the patients and their families referred to our care.

This issue of *Cancer in Ontario* is devoted to an examination of this "second" kind of cancer care within the OCTRF/OCI-PMH complex of institutions. Papers deal chiefly with initiatives in the large and complex sphere incompletely covered by the label "psychosocial oncology". They examine the spiritual, emotional, psychosocial and physical impact of cancer and the methods whereby we are attempting to address these issues.

A.D.G.

THE EXPERIENCE OF CANCER

The term, "experiential" disease, was introduced to describe the contributions to illness made by the patient's inner experience[1]. In doing so, Gold, Lumsden and Silverman draw attention to two phenomena taking place in the same space simultaneously: the objective disease—what the physician or scientist observes; and the subjective (personal) "illness"—what the individual experiences.

Cancer is many diseases and it is probable that each individual experiences his or her cancer somewhat differently. To honor the reality of the two "faces" of cancer, the objective and the experiential, *Cancer in Ontario* 1990 begins this symposium with testimony of a gifted human being, the late Dr. Robert Shepherd, who was variously a fighter pilot, a conservationist, a parent, a physician, a psychiatrist and a person with cancer. In the summer and fall of 1990, Dr. Shepherd, who was being treated for a highly malignant oropharyngeal cancer, published a series of essays in *Medical Post*, with the rueful title "The Advantages of Terminal Cancer". With permission, we publish a few excerpts from this remarkable testimony. Next we present a dialogue between Dr. E.A. Clarke the coordinator of Cancer Services for the province of Ontario and "Clara Rabine", a wife struggling to understand the system which her husband entered when he developed colon cancer. This section concludes with a reminder from Drs. Seravalli and Fashing of the tremendous importance to the dying patient of evidence of caring and person-to-person contact, especially with the physician.

The late Norman Cousins wrote eloquently of this relationship:

> *"Patients need and look for qualities in their doctors that go beyond technical competence. They want reassurance. They want to be looked after, not just looked over. They want to be listened to. They want to feel that it makes a difference to the physician, a very big difference, whether they live or die. They want to feel that they are in the doctor's thoughts. In short, patients are a vast collection of emotional needs. Yes, psychological counselors are very helpful in this connection, and so are the family and clergy; but the patient turns most of all and first of all to the physician. It is the physician's station that has most to offer in terms of those emotional needs. It is the person of the doctor and the presence of the doctor, just as much as—and frequently more than—what the doctor does that creates an*

environment for healing. The physician represents restoration. The physician holds the lifeline. The physician's words and not just his prescriptions are entwined in that lifeline…

…the physician's primary role [is] *as the keeper of the keys to the body's own healing system. To the students who read, and more important understand, the spirit and the essence of this* [message], *I would say, without hesitation or fear of hyperbole, you are medicine's future. You are also its only hope.*

I pray that you will never allow your knowledge to get in the way of your relationship with your patients. I pray that all the technological marvels at your command will not prevent you from practicing medicine out of a little black bag if you have to. I pray that when you go into a patient's room you will recognize that the main distance is not from the door to the bed, but from the patient's eyes to your own—and that this distance is best traveled when the physician bends low to the patient's fear of loneliness and pain and the overwhelming sense of mortality that comes flooding up out of the unknown, and when the physician's hand on the patient's shoulder or arm is a shelter against darkness.

*I pray that, even as you attach the highest value to your science, you will never forget that it works best when it serves your humanity. For, ultimately, it is our respect for the human soul that determines the worth of our science."**

J.O.G.

REFERENCE

1. Gold IJ, Lumsden CJ, Silverman M: Experential disease toward a structure for humane medicine. *Humane Med* 1985; **1:** 16.

---

*Norman Cousins: Foreword: Physician as humanist. *In:* Reiser DE, Rosen DH, eds. Medicine as a Human Experience. Rockville, MD: Aspen Systems Corporation; 1984: XV - XVI.

FACING CANCER*

R. SHEPHERD, M.D., *Dunkin, Quebec*

Since there is little future beyond today, I/we, my wife and I, live with remarkably few of the usual worries. Meditation comes more easily. Prayer too. But prayer now is more a waiting on God than petitions, as such, accepting that the patterns unfold as they must, the Divine Will being done on earth as it is in heaven. I find it difficult to pray for personal healing since I don't believe that nature (God) is either particular or sentimental, and who is to say that in the larger scheme of things the time for me is not now? The aim is a whole life, not necessarily a long one. So rest, enjoy and be tranquil.

I check out the forest of trees my children and I planted 25 years ago, and take great pride in the "forest of the Shepherds" that stands there, the wind sloughing through the great pine. A peregrine falcon swoops in for the kill in the field nearby, and not to be outdone, on the way back a little later, near sunset, the great horned owl announces his nightly hunt. When the time comes to head off on the long paddle, I'll be proud of the Land Trust, and comforted to think the peregrine falcon will still have large tracts of forest to call its own.

ONE ADVANTAGE ANYWAY!

...terminal cancer streamlines the choices. The fact that nothing can be done to alter the prognosis lifts you at once out of the appalling cleft stick so many people find themselves in with treatable cancer... The choice was no longer mine; the option for quality living had been made on its own. It's largely a matter of control, of being in charge. Once you hand over that crucial sense of mastery into the hands of the experts, they call the shot, not you. They are the master then, you the slave, passive, obedient, even

---

*These passages are extracted from a series of articles written by the late Robert Shepherd, a physician and conservationist in the weeks before his death from cancer on September 29, 1990. The articles first appeared in *The Medical Post* between July 24 and November 20, 1990. We are deeply indebted to Derek Cassels, the editor and Frank B. Lederer, the publisher for allowing us to share Dr. Shepherd's work with our readers. Reprints of these series may be obtained from:

Medical Post
777 Bay St. 5th Floor
Toronto, Ontario
M5W 1A7

docile; a patient. But with the terminal label you remain in charge, you and your body as one, the way it's always been.

NO ALZHEIMER'S, EITHER

"That's another advantage of going a bit early, no what-was-that-name-now? or I-know-that-person-but-can't-remember-who-they-are. No doddering old age with leaking bladders, failing memory, failing sight and just the hint—if you have the wit to see it—of the endurance in your loved ones' eyes. They love you, of course, but the old man takes a long time dying. This way there is a clear wish on their part for you to stay a little longer, don't go just yet, let the grandchildren know you better, let us lavish you with the love and understanding we've always wanted to do but couldn't quite find the time, the opportunity, or you were not open to it then, you the strong one, successful, driving on. But now we can reach you and love you, so please stay a little longer so that we can love you some more."

Time to meditate more, pray more, waiting on the divine process to unfold as it will. Time to love more and be loved more by those who could not or would not (yourself included) let love and grace flow over and around you, uplifting, healing, moving on. So you cry together and laugh together, and yearn for more even while knowing that mourning starts the day you are born, and ends only when the gut releases memory at last. The textbooks say mourning takes from six months to a year, but that's nonsense; it takes longer than that, sometimes forever. What I mean is people who die suddenly miss a lot of all this, including the chance to mourn each day a little as you go along.

CANCER A COLLECTIVE ILLNESS

You soon discover, for example, that cancer is a collective illness and not a private matter as you had surmised at the start. People feel free to call at any hour of the day or night, inquiring how you are, or to visit without notice, bearing gifts, examining you carefully on arrival. They say: "You look better than I thought you would," making you feel vaguely guilty and suggesting the judicious use of eye-shadow for the next time. Since dying is heavily into theatre, you have to look your part.

Together with the discovery that cancer is a public affair…you perceive early that you have to fight back whether you want to or not… The important thing is that the moment you get the diagnosis you gird yourself for battle. Nothing less will do. Any attempt to accept dying as part of living is squelched from the start... The reaction is one of mutinous disorder among loved ones and friends. No treatment? Out of the question! Attack, attack! In fact, at times the whole thing seems harder on them than on you, bless their hearts.

THE POWER OF POSITIVE THINKING

Which brings us to the imperative of positive thinking in the call for healing energies. Two bestsellers by doctors lead the field, "Getting Well Again" by Dr. Carl Simonton...and his psychotherapist wife Stephanie Matthews, and "Love, Medicine and Miracles" by Dr. Bernie Siegel. Health is an attitude of mind, and good health or bad health are not what happens to you, your soma or psyche, but how you react to whatever happens to you. In our materialistic, "practical" approach to health care we often overlook this fact. Not that science lacks a place or that scholarship need not be rigorous, but simply that sickness and healing are mysterious forces not yet within the purview of the rational mind, and the fact that you can't prove it rationally does not mean it doesn't happen. As a doctor friend of mine who had cancer said: "Statistics are important but not for individuals. You could be the exception to the rule." To be fair, books (like those of the Simontons and Siegel) bring strength and reassurance to those in early shock from the cancer diagnosis, and provide some measure of the self-mastery without which the sick lose control and wait, generally depressed, at the beck and call of doctors and technicians. They provide insights into the traps to avoid, the benefits to go after, and training in the use of guided meditation or biofeedback techniques of undoubted value in the handling of illness.

FACING PAIN

Try to stay part of the whole, part of the main; keep things in perspective. Try to see yourself as your wife sees you, as your children and neighbours see you. You are not the only one to have pain, remember; not the only one to die.

Pain has to be felt to be known, no amount of description, however vivid, comes close to the experience itself. Pain is what the sufferer feels, no more, no less. Hippocrates said: *"Divinum est opus sedare dolorum"*, divine is the work of subduing pain... Cancer patients suffer pain which is both physical and psychological... Psychological pain emerges from the depression of mood which so often accompanies the illness, especially in those who live alone. To die in a solitary room with little or no support, often without food or medical care, is an agony not to be wished on anyone.

Many patients unprepared for the fatigue common to cancer find themselves prone to despair—as I was at first—when lassitude urges them to choose bed in preference to food, company, sex or other pleasures. If you have been an active person all your life, and you feel your energies drop, your weight slide, your appetite vanish, that's suffering however you cut it.

SO WHOM DO YOU TRUST?

"That node has almost doubled," the radiation therapist said, measuring with a ruler. A voice inside me said: That's my lung you're talking about there, eh? My future you're measuring. Careful. Frankness in the medical profession is one thing—a welcome change from the evasions of the past—but discussion of technical details in the presence of the patient is quite another. The rule is the rule: Don't tell patients more than they want to know, don't speculate unless asked to, and don't forget what you intimate speaks louder than words. To a radiologist looking at an X-ray who says "It's aggressive," nodding vigorously, the next question is: "So, do I go out and shoot myself next week?"...I had never honestly considered such questions before—doctors are doctors, after all, they do their jobs. The idea that they might be crushing the soul in the courts of the flesh was new to me, and as for how far my own doctors had explored their vision of the soul, whether they prayed or not, or had any spiritual orientation toward life and death, these somehow did not seem appropriate subjects to raise,... But if you start doubting your doctors when you are sick who then do you trust when the tides of fear come lapping at your door? For cancer is a lonely place with many questions, many doubts. Your family and friends give you all the help they can, and incredibly sustaining it is, but they are not professionals, they don't know about things like cancer, its tempos and habits, its history and inclinations... They don't have the information, and when all's said and done, what sick people need most is clear information honestly given, reliable facts garnered from a wide range of experience, all threshed out as far as is possible, through the exacting mills of scholarship and science. Anecdotes are not enough.

SOME ACTION YES, BUT WHAT?

To remain passive or indifferent in the face of cancer is clearly not responsible, but to strive against the natural pattern is equally out of line. The river is the force, the river does the work; rest on the power of the river. Our task, like the Amerindian in his canoe, is to remain alert, paddle in hand, ready to shift a little here, move a little there to make our passage easier, more efficient.

We are important but minor partners in the great drama of existence, and who are we to suggest, as these books do, that we may by effort of will, hold back the river, or alter its course or destination for ourselves in any significant way. Who am I to say that it's not time for me to go? Who am I to question, far less to understand the inscrutable will of God? No, no, let me paddle well into the stream and rest there as we move, fully aware, down to the sea, sharing with the antlered buck at the river's edge in their evening vespers: Great Gitchimanitou, Lord of the river and sea, lord of the forests and winds, look with favour on this thy creation, and let grace and gratitude attend us.

FACE TO FACE: THE RABINE-CLARKE DIALOGUE*

E.A. Clarke, M.B.,B.S.**, *Toronto, Ontario*

Clara Rabine lost her 47-year-old husband, Wilhelm, to cancer of the colon on June 27, 1990. In her struggle to secure the best available treatment for him, Mrs. Rabine had to deal with many anxieties, concerns and frustrations because, like many other people, she was unfamiliar with ways whereby patients can obtain cancer treatment and support in Ontario.

Some months after her husband was diagnosed as having cancer, Mrs. Rabine contacted Dr. Aileen Clarke, Cancer Co-ordinator for the province, and they had continuing discussions. The following dialogue reflects some of the points raised in the discussions.

Mrs. Rabine: What do you do in your appointment as Cancer Co-ordinator for Ontario, Dr. Clarke?

Dr. Clarke: I'm an advocate for cancer. As Cancer Co-ordinator, I endeavour to influence the co-ordination and integration of cancer services within the Ministry of Health and between the Ministry and other organizations and individuals. I try to keep in touch with the issues that relate, not only to the treatment of patients with cancer, but also to the prevention and diagnosis of cancer and to the support of patients with cancer and their families.

When I become aware of a particular issue, I work with people in the appropriate branches of the Ministry of Health and other ministries, bringing together individuals who have responsibility for some aspect of the issue. For example, I am concerned about the shortage of radiation therapy technologists in Ontario and became chairman of a committee developing new models for the education of these technologists. Representatives from several branches of the Ministry of Health and the Ministry of Colleges and Universities, as well as health professionals, served on the committee.

R: How does a person find out they have cancer?

---

*Clara and Wilhelm Rabine are pseudonyms. However, the events described herein are true.

**Cancer Co-ordinator, Health Programs, Ontario Ministry of Health.

C: Generally, an individual will notice a lump, difficulty in breathing, speaking, or swallowing, cough, pain or some other symptom that takes him/her to the family physician. The physician will take a history, do an examination and may order tests or, if there is a strong suspicion of cancer, the patient may be sent directly to a specialist for further investigation; in other circumstances, such as a lump in the breast, the patient may go directly to a surgeon to establish a diagnosis.

Usually, diagnosis is not made on the first visit to a physician. After investigation, such as blood tests and others, the next step is to obtain what is referred to in the medical profession as a "tissue diagnosis". If possible, the tumor, or part of it, is removed and examined by a pathologist to establish whether it is cancer and what type. In some cancers, the type of treatment will depend on the characteristics of the cells under the microscope.

R: What happens when a diagnosis of cancer is made?

C: A decision might be made to try and remove the cancer completely by surgery. If the cancer has spread and cannot be completely removed, a multidisciplinary team, which may include a surgeon or specialist in radiation therapy or chemotherapy, will decide whether to offer chemotherapy and radiotherapy or a combination of both. Even if an operation isn't possible or the cancer cannot be completely removed, the patient's disease may be held in check for a considerable time by chemotherapy or radiation. Radiation is only available in Ontario at the Princess Margaret Hospital or at one of the eight Regional Cancer Centres of the Ontario Cancer Treatment and Research Foundation. Chemotherapy is given at these locations but is also available from medical oncologists (cancer specialists who use drugs and other agents to treat cancer) who are associated chiefly with teaching and large community hospitals.

R: My husband had a major operation to remove his tumor. Our family physician assisted with the surgery and told us that the tumor had been removed but he expressed concern that, because it was a large tumor, they had not been able to remove all of it. However, the surgeon told us that he was pleased with the result and, following review of the pathology report, told us everything was fine. He did not tell us that, because of the size and location of the tumor, there was a good chance that the cancer would recur. Our family physician was present during the operation and realized that the cancer might recur but later told us that, because of professional protocol, he didn't feel able to tell us at the time of the surgery. Why was that?

C: This is a difficult question. Having referred Wilhelm to a surgeon, your family physician might have felt that it would have been inappropriate for him to comment further. I believe that was most unfortunate. Family physicians, with their knowledge of patients and their families, should be in the position to ask surgeons to give the whole story—the good news and the bad news, but this is not always possible.

R: Would you like to see a more full and comprehensive dialogue between the family physician and the specialist, Dr. Clarke?

C: I would like to see on-going, free dialogues between family physicians and all specialists to whom a patient is referred, as I believe it would be to the patient's benefit. All physicians caring for the patient would then be aware, on a regular basis, of the patient's progress.

R: In general terms, Dr. Clarke, what should a patient be told when a diagnosis has been confirmed?

C: I believe a patient should be told as much as they wish to know. Cancer is a complex disease and the course cannot always be predicted. Some patients don't want to know very much, they don't want to be involved in decisions about their own treatment. They prefer to be told just what has to be done and no more. On the other hand, the public receives a great deal of information (and misinformation) about cancer, and so some patients ask many questions so that they will be well informed. It is important to keep to a minimum the number of times the patient or family are left in the position of saying "if only I had known in time"—so that they could make a will, send for a distant relative or patch up a long-standing quarrel. In retrospect, if you and Wilhelm had recognized earlier that he probably had a fatal disease, then I'm sure you would have dealt with events differently, knowing that he was unlikely to be cured.

R: Should the physician take the initiative by asking patients how much they want to know?

C: Probably, yes, but this is not always possible.

R: Why?

C: It depends on both the physician and the patient. As I said earlier, some patients wish to be informed and others do not. In the same way, some physicians may not feel comfortable giving patients the detailed information needed to make such decisions. Generally, there is not an emphasis on joint decision-making in the general teaching in medical schools. Nevertheless, there are, obviously, physicians who do keep their patients well informed. You told me yourself about one physician who answered all your questions honestly and fully "in plain English". He made it clear he wasn't an expert. He told you if you wanted more information you would be best to talk to a specialist.

R: Most of what I learned about Wilhelm's disease I learned from books that I got from the library. Each visit I prepared specific questions regarding Wilhelm's treatment and care. The answers I received were vague at best and sometimes very worrisome because I was told that "I really didn't want to know". How do patients obtain information about cancer other than from their family physician or specialist?

C: There are organizations that endeavour to provide authoritative information to cancer patients and their families. The Canadian Cancer Society, which has divisions in every province, has spent much time and effort over the years in developing programs to disseminate such information. You told me that you and Wilhelm benefited from one of these programs, 'Living with Cancer'.

R: If the patient or the family are not happy with the information they are receiving or would like another opinion, what should they do?

C: A patient or his family can say quietly but firmly that they would like more information, that they would like to participate in the decision-making process and, if they are not happy with the response they receive, they are entitled to seek a second opinion. Nowadays, seeking a second opinion is not regarded as showing a lack of faith in the physician who gave the opinion. However, many patients fear that, if they ask for a second opinion, the attending doctor may refuse to look after them any longer.

R: Are most physicians now comfortable with a patient or family who asks for a second opinion?

C: Yes, but patients may still be afraid to ask, particularly if they are not close to the physician. Also, you may be ready to ask on a very busy day when the physician doesn't have the time needed for a detailed explanation.

R: With all the media attention to "breakthroughs", do you believe that the public has inflated expectations about what the health-care system can do?

C: Yes. There is no mechanism in place in the print and electronic media to ensure that new discoveries are put in a proper context or perspective so that it will be plain to the reader, listener or viewer that the "breakthrough" may need years of further research before it can be applied to the prevention or the treatment of cancer.

R: Do many patients enter their cancer experience expecting physicians and surgeons to be miracle workers and effect a cure?

C: Yes, I believe so.

R: Is that a problem?

C: Yes, because treatment has only had a dramatic effect on survival in some rare forms of cancer, such as childhood leukaemia and testicular cancer. There has been a small improvement in the survival at five years for the more common cancers. The new treatments that you hear about in the media do improve the quality of life of those who have cancer and that is most important.

R: At one point I believed that, if Wilhelm had been referred to a cancer centre sooner, his life might have been saved. What do you think?

C: Your husband had colon cancer, that is, cancer of the large bowel. Eventually you found out that it was an irregular cancer that had gone through the bowel wall and involved the vena cava (the large central vein in the abdomen) and so the possibility of cure was remote. Radiation rarely is successful in curing this type of cancer and it is unlikely that the delay would have caused your husband's death. There was some shrinkage of the cancer from the radiation treatment and that may have prevented other problems developing.

R: At one point when we were trying to get radiation treatment, I saw five different doctors in five weeks. Can we not streamline the system so as to avoid unnecessary visits and keep to a minimum the delay between diagnosis and treatment?

C: You have identified an important and difficult challenge for the cancer system in Ontario. Part of the challenge is that the number of cancer patients is increasing rapidly due to the increase in the number of people living in Ontario and the fact that many people are living longer and reaching the age at which they develop cancer. It has not been possible to increase the financial and other resources allocated to cancer care in proportion, therefore, there are inefficiencies. However, it is hoped that, in spite of the limited resources, with doctors, patients, government and others working together, methods will be found to correct the faults of the system and provide complete care to cancer patients and their families.

R: If the government cannot assign more resources, can the system be improved in other ways?

C: Yes, we can make better use of the resources now available. Possibly, some of our efforts that are going into treatment, which will not necessarily cure the patient, could be allocated to increasing facilities for the relief of pain and other support services.

R: I'm still concerned that Wilhelm was not referred to a cancer treatment centre for radiation therapy quickly enough. I believe we could make the referral process more efficient if each hospital had a cancer co-ordinator. The cancer co-ordinator could provide a link between the hospital and the treatment centre. What do you think?

C: There are 244 hospitals in this province so I do not believe that you need a cancer co-ordinator at each, except, perhaps for the teaching and other large hospitals. Because cancer is the leading cause of death for people under the age of 75, it may be possible to justify the appointment of an individual, not necessarily a physician, as a resource person to whom patients can be referred. Hospitals under a certain size could share a cancer co-ordinator through a network.

R: How could initiatives to improve the life of cancer patients and their families be put in place?

C: In Ontario, the impetus might come from a number of organizations; the specialized cancer centres, namely, the Ontario Cancer Treatment and Research Foundation and The Ontario Cancer Institute, incorporating Princess Margaret Hospital; the Ontario Division of the Canadian Cancer Society and other volunteer organizations and self-help groups. It could also come from a co-ordinated government approach, which would involve these and other key stakeholders in the province.

R: Any such initiative would certainly have helped Wilhelm and myself. My husband's last visit to the cancer treatment centre will be etched in my memory forever. We arrived early. We waited for over an hour and then saw a doctor we had never seen before. The doctor wasn't sure why we were there. He gave Wilhelm a cursory check and then told us to come back in two months. I was sent home with a dying man and no instructions. Because I worked in a hospital, I did know about home care but was unable to obtain it sufficiently quickly and, less than a week later, Wilhelm died on a stretcher, waiting for a bed in a hospital near us. Is there anything that could have prevented the way in which my husband died?

C: Unfortunately, it is not always understood, when the doctor realizes that nothing more can be done, that there generally is a mechanism in place to support the patient in the days and weeks before the patient dies. That lack of co-ordination was very obvious in your case. A major national initiative, Cancer 2000, sponsored by the Canadian Cancer Society, the National Cancer Institute of Canada and Health and Welfare Canada is developing strategies for co-ordinating efforts in all areas of cancer control. It is a two-year consultative process involving many people across Canada.

R: As Cancer Co-ordinator, do you feel hopeful about the future care of people with cancer and their families in Ontario?

C: Cancer 2000 has answered this question very well. Canada, including Ontario, has one of the best cancer control systems in the world. This is the result of government providing resources, and the dedicated efforts of physicians, health care providers, career scientists and volunteers. Even so, most of the individuals who have created this standard of quality believe that we can and must make significant improvements. The task of prevention, diagnosis, treatment and aftercare is enormous. Working together, we can improve the care given to people with cancer. However, everyone needs either, like you, to speak out or, like myself, to listen and respond to people like you. Mrs. Rabine, thank you for sharing your experiences with me and for helping me put our discussions in writing.

ACKNOWLEDGEMENT

The authors wish to thank Timothy H. Godden for his assistance in arranging this dialogue.

PHYSICIANS AND THE DYING: SEARCHING FOR THE HUMAN CONNECTION*

E. SERAVALLI, Ph. D.** and J. FASHING, Ph. D., J.D.†
New York, N.Y.

Patients with an advanced fatal illness want to talk about themselves, their feelings and their disease to their physicians, who often are not ready to listen. The dying look forward to the doctor's expressions of concern about impending death and a doctor's withdrawal robs the patient of an essential reassuring presence[1].

Behaviour, which denies reality, is very painful for the terminally ill, who perceive it as a rejection—a premature severance from the world of the living. This breach, created by everyone's withdrawal, is the result of a profound sense of inadequacy, of not wanting to confront an event, which is inherently frightening, and of a growing sense of estrangement on the part of the patient. Everyone feels that anything said is hopelessly banal and anything done, necessarily superfluous. What we have come to realize is that any word, any gesture, whatever is said or done, is meaningful for the dying as long as it expresses a human connection and strength in dealing with the real situation.

Near death, the main fear for the terminally ill is not impending doom, but the threat of abandonment and the prospect of intolerable pain. Dying patients need to be reassured by doctors that the moment of death is not painful and the doctors have the capacity to cope with unexpected problems. They need their doctors to dispel uncertainty and fears, not so much of death, but of the hardship of dying with its catastrophic physical breakdown and its unknown feeling. A terminally ill writer showed how the natural fear of death can be transformed into deeper anxiety when there is no communication between the dying and their physicians: "Always more sick, always more silent, always more lonely...with the bitter taste of death in my mouth". In these moments the physician, who stands fast and offers empathy, can transform lingering fear into strength in the preparation for death.

---

*This passage, from a paper of the same title, is used with the permission of the author and the publisher, the Canadian Medical Association. The complete paper will appear in the summer 1991 issue of *Humane Medicine*.

**Department of Anesthesiology, Beth Israel Medical Center, New York, N.Y.

†Division of Social Science, State University of New York, Purchase, N.Y.

We have observed that, in the later stages of the dying process, patients are motivated more by their own emotional needs than by the demands of the outside world. As time passes and the disease worsens, the dying concentrate even more on their inner world and less and less on the outside—progressively detaching themselves from the world of the living. When this occurs, the dying have come to terms with their mortality. They are ready to embrace death.

The following letter, written by a 47-year-old professor eight days before her death from leukemia, eloquently emphasizes this point.

> ...Today is a day of shortness of breath... and little optimism because my leukocytes, after being artificially augmented with transfusions of leukocytes from others and bone marrow from still others, are diminishing at a very rapid rate. I feel that I am becoming boring to others as well as to myself. I see my husband almost physically shrink before each fresh disappointment...I don't think I will make it. This month's experience of frantic treatment has not prevented my getting worse rapidly...And now, after a month that has been full of problems and my being in bed constantly, I cannot even imagine the way I was a month ago. I can assure you, however, that I am not terrified. On the contrary, I am surprised at my serenity...

If I ever make it, the experience of this period would be all positive for me because of the warmth of your friendship—the friendship of so many of you—your generosity, that of my physicians, that of the known and unknown donors of blood and bone marrow, have all been such a revelation of human goodness so great and precious that I can even take out "if I make it" and say instead: "it is worth paying for with my life"...[2]

This profoundly touching document unequivocally expresses how a person can rise above the fear of death if bolstered by the care and compassion of physicians and friends. For a serene acceptance of death, physicians play an invaluable role because dying patients, in spite of their worsening physical condition, want to trust their doctors, their counsel, and their healing power. Thus, when death cannot be postponed any longer, compassionate physicians can shift their attention from medical intervention to helping the patient to face death with a minimum of suffering.

The woman, who wrote the letter above, was bolstered by the care and compassion of skilled physicians and she remained in command of her life until the end. Her serenity represents a triumph of the human spirit over the outcome of the illness.

In documents of dying people and in their verbal communication, it is not uncommon to find that the dying process is identified neither with their life for with their disease. Rather, it is a period in which the dying change their perception of life and of themselves. Dying is an inward process in which a person gains new insights that may alter their sense of connection with physical reality. Thus, dying people may be quite different at the beginning of the process from what they become at the end. This aspect of the dying process is extremely complex and little understood. Too often it is associated with a change in the attitude of attending physicians, who have difficulty in coping with the reality of death.

The dying patient and the process of death highlight the two facets of the medical profession: that related to genuinely humane care, and that of professional effectiveness.

When physicians become willing participants in the emotional aspect of the process of death, they do not perceive the death of suffering patients as a personal defeat. In the words of Sir William Osler, such a physician will have learned "...to look on death with mingled feelings..." and will have understood that suffering patients with incurable illness welcome "...death that comes with friendly care"[3].

How much personal and professional growth might there be if young physicians would spend a few minutes with the dying patients listening, ***really*** listening, to their words. They might discover the therapeutic power of their compassionate attitude. They might learn to dissipate the distress that comes when very sick patients do not know what is happening. They might help to break the barrier of silence that often surrounds the dying, who have the same needs, hopes, fears and instincts as all of us. In their hearts, and in their sometimes unrealistic hopes, dying patients need a human connection and expect words of encouragement and compassion from their physicians. At this critical juncture, sensitivity to human needs enhances the significance of medical science and expresses the highest values of the medical profession.

REFERENCES

1. Seravalli E: The dying, the physician, and the fear of death. *N Engl J Med* 1988; **319:** 1729.
2. Enriques-Agnoletti A: Letter to a Friend. Personal document. 1959.
3. Osler W: Counsels and Ideals From the Writings of William Osler. Boston: Houghton Mifflin, 1905: 260.

PSYCHOSOCIAL ONCOLOGY — AN OVERVIEW

A.D. GINSBURG, M.D.*, *Kingston, Ontario*

Despite significant progress in the diagnosis and management of cancer, it remains a dread disease. The emotional distress, which the diagnosis evokes, demands that those who care for patients with cancer do so with the utmost compassion and caring, and with a constant awareness of their special vulnerabilities and needs.

In this essay, from the perspective of a cancer centre director, I shall provide an overview of the supportive care services currently available, draw attention to some problems, and suggest some solutions.

Supportive Care Services Currently Available

It is by no means clear what the supportive care needs of cancer patients are or how they should be met. For convenience we can classify perceived needs under such headings as physical, emotional, social, and informational. These, elaborated in Table I, have served to guide supportive care developments in Kingston but they have not been validated by specific study.

These needs are addressed in a diverse manner by the patients themselves, their families and their friends, and the family physician. In addition a number of community agencies provide supportive care to patients with malignant disease. These comprise:

Regional Cancer Centres. All levels of staff are, or should be, attuned to the special needs of cancer patients. In the late 1970s and early 1980s, the centres began to appoint staff specifically concerned with the provision of such supportive care, namely social workers, nurses, psychologists, psychiatrists, clergy, nutritionists and even a consultation team. The numbers of these special persons vary from a high of 4.5 at one centre to none at others.

These staff provide two general types of service: assessment and then referral to the appropriate agency; and specialized counselling to patients and families, comprising pain and symptom control, individual and group support, behavioral therapy and bereavement follow-up.

---

*Chief Executive Officer, Kingston Regional Cancer Centre; Vice-President OCTRF.

The Canadian Cancer Society. This voluntary organization will provide transportation for therapy; some supplies such as ostomy or incontinence devices for patients who are not on home care programs; financial assistance—if hardship exists—in the form of $25 towards the cost of a wig, $125 towards the cost of a breast prosthesis, and the costs of analgesic and antiemetic drugs; homemaking to a total of 80 hours; emotional support through a number of programs such as CanSurmount; and educational programs.

Hospices. These organizations are entirely voluntary. They work in conjunction with family physicians or other physicians primarily responsible for the patient's care and provide a program of care to people whose diseases will not be cured.

Registered nurses are on 24-hour call to provide assistance with symptom control, psychosocial needs, communication between patient, family and friends, financial needs and spiritual needs. Community volunteers are co-ordinated and trained to provide family respite, special foods, trips, outings and social interests.

The Home-Care Program. This program enables many patients to stay at home. Once patients are accepted into the program, they have access to:

- The Victorian Order of Nurses (VONs), and, in Toronto, St. Elizabeth Visiting Nurses Association (SEVNA). These nurses may visit the patient at home from once a week to four times a day. They will give injections, change dressings, provide skin care and bed baths, and monitor symptoms. They will also liaise with the referring physician.
- Physiotherapists, who will teach the patient and the family concerning body mechanics and range of motion exercises.
- Public health nurses, who will provide emotional support and maintain close observation.
- Occupational therapists, who will assess for and provide the assistive devices, and modifications to bathrooms, kitchens, cars, etc.
- Homemakers, who will provide light housekeeping in the form of meal preparation, laundry and personal care. Resources are finite; they are provided at 4 hours per day in the first month to a total of 80 hours and at 2 hours a day in the second month to a total of 40 hours.
- Nutritionists, speech therapists and social workers.
- Equipment rental.

Problems in the Provision of Supportive Care

Despite the impressive array of services, a number of problems need to be addressed. Thus:

- The OCTRF has no overall policy with regard to the provision of supportive care to patients with malignant disease and their families. It is not clear whether the OCTRF has accepted this responsibility as an integral part of its mandate, and, if so, to what degree. A crude calculation suggests that perhaps 1% of the overall OCTRF budget is committed to the salaries of staff primarily concerned with these areas. Also it is not clear, when we are developing OCTRF and Centre priorities and budgets, how we should compare such services as surgery, radiotherapy and chemotherapy to the provision of supportive care.
- We have only rudimentary processes to assess the need for psychosocial support. Referral to the psychosocial team is random. Patients are referred on an ad hoc basis, often only in response to a crisis.
- Most of us, even those with specialist credentials in some aspect of supportive care such as psychiatrists, psychologists, oncologists, nurses, technologist, social workers or the clergy, have had little or no formal training with regard to supportive or palliative-care practices in oncology. Most of our abilities have been acquired "on the job" and are learned randomly with varying degrees of enthusiasm and ability.

Dr. Wesley Boston, recently appointed as the Director of Palliative Care Services at the Kingston General Hospital, made the following observations:

> "Clinical clerks lack elemental knowledge of symptom control, and are very uncertain of how to address the emotional, social and spiritual needs of cancer patients and their families.
>
> Some of the more senior housestaff have a distressing indifference to the needs of their dying patients and their families, and a remarkable resistance to accepting that some of their patients will die.
>
> Attending staff are, for the most part, distant from the details of daily management of terminally ill patients, are reluctant to provide leadership and are relatively unfamiliar with currently accepted practices of good symptom control. They do not provide good role models in this area."

Nurses and technologists express frustration at their inability to meet the needs of their patients for supportive and palliative care. Physiotherapists, occupational therapists, social workers, pharmacists, nutritionists and clergy all express a desire for further training and greater involvement.

Volunteers from all walks of life are enthusiastic but need careful selection, training and supervision.

- Many of our treatment strategies have not been thoroughly validated.
- There is little or no integration within or between the various Centre, community and hospital services and it is even possible that territorial jealousies exist.

Proposals to Enhance the Provision of Supportive Care

I offer the following suggestions in the hope of enhancing the supportive care services available to patients with cancer, who are referred to a regional cancer centre.

1. In the first instance, society—represented by the Ontario Ministry of Health and the Board of the OCTRF—should make a clear commitment to the concept that psychosocial care of the persons and families affected by cancer is as important as the treatment of the disease. These bodies should state clearly that the provision of optimum supportive care definitely is within the mandate of the Centres. Appropriate funding should be provided.

2. Research is essential to ensure that the care provided is appropriate. While needs for such care are perceived and caregivers display much goodwill and good intentions, we need to learn a great deal more before we can meet these complex needs. Much research must be undertaken to delineate the specific needs of different patients and groups at different phases of the illness. We must develop and validate appropriate assessment tools, we must develop and refine our interventions, and thoroughly validate these before their wholesale adoption. These measures will require the same rigorous evaluation that is applied to any new therapy employed in the management of cancer. It follows that granting agencies must be brought to recognize the importance and credibility of such research.

Pending the results of such studies, I offer the following empiric suggestions:

- Each Centre should ensure a warm and welcoming environment:

i) Physical facilities should be made pleasant and comfortable by the addition of suitable, pleasing furniture and other amenities.

ii) All Centre staff should receive orientation and frequent reorientation concerning the special vulnerabilities and sensitivities of cancer patients and their families. Ideally, interactions with any staff person will be warm, welcoming and comforting. I wish to emphasize that all Centre staff have important contact with patients—receptionists, secretaries answering the phone or making appointments, nurses, technologists, pharmacists, porters and physicians all have opportunities for positive patient interaction. Ideally, in this regard, staff morale should be high and staff should not be harassed or overburdened—thus they will have both the time and the motivation for positive supportive interaction with their patients.

iii) Support staff should expedite each initial consultation and appointment in these usually anxious patients. Similarly, they should expedite the necessary investigations and transmit the results to the patients promptly and in a considerate fashion.

iv) Each centre should develop appropriate mechanisms so that patients and their families are oriented rapidly to the Centre and to the principal personnel serving them - perhaps even before their visit.

v) Patients should be seen punctually and, ideally, by the same physicians, nurses and technologists, as they attend for subsequent treatment and follow-up.

vi) Facilities should be adequate so that therapy is never delayed for nonmedical reasons.

One cannot overstress the importance of these initial interactions:

> "It is during...this initial encounter...that the patient and family begin to place their trust, faith and confidence in the physician [and nurse, and technologist] - truly the golden moment."
>
> L. Robert Martin, 1982

Particular awareness and sensitivity is needed at other milestones—during treatment, when treatment is completed, during remission, at the time of first relapse, during the chronic phase of the illness, during the terminal illness, around the death, following bereavement.

- We need to develop effective tools so that we can assess patients' needs in a formal, planned and continuing fashion and thus provide promptly the appropriate interventions. Such assessments and interventions must be geared not only to the patient, but to the spouse, to the parents of young patients, the children of older patients, and the parents of older patients—a much neglected group. We must demonstrate that our interventions are appropriate and effective.
- We must provide patients with the necessary information about their disease and its treatment.
- Counselling services are now available—referral to an appropriate agency; individual counselling by the family physician, a social worker, psychologist, clergyman, psychiatrist; group therapy; and drug therapy. It is important that we tailor the intervention to the patient and to the circumstance; and be prepared to show that these are effective.
- Available resources must be integrated and co-ordinated.

  In her "needs study" in Prince Edward Island, Mary Vachon noted that "...most people requiring practical assistance received it from their families and friends".

  How do we interact with these primary caregivers so as to maximize the support they provide? How may we provide them with the best available information concerning additional resources?

  In our own experience, regular meetings of Centre staff, family physicians, representatives of the major community agencies and trained supportive care personnel are most useful in planning and integrating patient management in light of identified needs. In this regard, the addition of a home care co-ordinator in our Centre has proved invaluable as has regular telephone communication with the family physician.
- We should ensure development of the necessary skills by providing well-trained instructors and suitable educational facilities.

  As much skill is needed in speaking to patients and families with cancer as in performing cardiac surgery. Such dialogue requires knowledge, judgement, understanding and sensitivity. One must decide, preferably in advance, what to say and what not to say, how much to say, how to say it, to whom, by whom and when.

Essential to good communication is knowledge, and not merely intuition, concerning available resources, techniques suitable for symptom control, ways of communicating and ways to counsel at the various milestones. Each of us has some information in this regard, but these are fruitful areas for carefully designed and executed research.

The knowledge and skills of present and future staff must be transmitted to trainees and practitioners with the same care as is devoted to other clinical training.

Conclusion

Technology is assuming ever-increasing importance so it is heartening to be able to harness such technology in an environment characterized by the human values of kindness, concern, empathy and decency. It is a privilege to work with colleagues of all professional backgrounds whose overwhelming desire is to improve the quality of life of our patients and their families and to facilitate their adjustment to the altered reality represented by cancer.

TABLE I

PATIENT NEEDS FOR SUPPORTIVE CARE*

PHYSICAL NEEDS

1. Detection and Control of Physical Symptoms Consequent on the Cancer and/or Its Treatment:
   - Pain
   - Weakness and fatigue
   - Anorexia
     - nausea
     - vomiting
     - difficulties with diet
   - Thirst
   - Abnormalities of bowel movement
   - Difficulties with micturition
   - Difficulties sleeping
   - Cough
     - dyspnea
     - hemoptysis
   - Any other specific complaints

PSYCHOLOGICAL NEEDS

1. Detection of, and Attention to, Emotional Concerns:
   - Fear
   - Distress
   - Anxiety
   - Depression
   - Grief
   - Anger
   - Guilt
   - Abandonment
   - Dependence and lack of control
   - Helplessness

(Fear of recurrence is noted particularly in the PEI study.)

2. Detection of, and Attention to, Psychiatric Illness
3. Attention to Spiritual Needs
4. Detection of, and Attention to, Sexual Problems of Both Patient and Spouse.

---

*Schema used at Kingston Regional Cancer Centre to guide comprehensive care.

TABLE I (Continued)

PATIENT NEEDS FOR SUPPORTIVE CARE*

SOCIAL NEEDS AND CHANGES IN LIFESTYLE CONSEQUENT ON THE DISEASE AND/OR ITS TREATMENT

1. Attention to Social Needs:
   - Daily home help
   - Shopping
   - Transportation
   - Child care
2. Awareness of, and Attention to Family Stresses Involving:
   - Spouse
   - Children
   - Parents
   - Extended family with provision of family relief when necessary
3. Awareness of, and Attention to Financial and Legal Needs Involving:
   - Financial circumstances:
     - work situation
     - pension
     - disability
     - insurance plans
   - Wills:
     - power of attorney
     - other legal needs including "living wills"
   - Drug costs, cost of appliances
   - (Work-related problems were noted particularly in the PEI study.)

INFORMATIONAL NEEDS

1. Attention to Needs for Cancer Information:

   Patients and their families with regard to:
   - the nature and amount of information desired about the illness, its prognosis, its treatment and the side-effects of treatment;
   - the services available in the community to patients and their families:
     - the immediate community
     - the general community

NEEDS OF CANCER PATIENTS IN ONTARIO

J. LOVERIDGE* and M. ISTILOGLU**
Toronto, Ontario

A recent survey commissioned by the Canadian Cancer Society Ontario Division, provides a wealth of new information about the physical and psychosocial needs of Ontario cancer patients and their families—needs which they themselves have identified. This unique study will assist the Society and other agencies to help patients and their family members cope with the effects of cancer.

This study, a signpost to future directions in service delivery, points to the kinds of non-medical support those affected by cancer say they need most, and it strongly endorses the Society's commitment to expand patient services. Some of the 17 recommendations have far-reaching consequences; for example, one proposes the Society gradually withdraw financial assistance as the government assumes greater responsibility in this area. The report also urges the Society to provide more information and greater peer support. The Society's strength is its volunteer network and this network is well suited to the delivery of these services.

This survey, "The Needs of Ontario Cancer Patients: An Assessment", was launched in the spring of 1989 and a final report received by the Division in May 1990; it was conducted by Price Waterhouse and Diane Abbey-Livingstone & Associates under the guidance of a steering committee of volunteers and Society staff members.

The survey examined several key service areas:

- the needs of patients and their families at different times—at diagnosis, during treatment in the event of recurrence, and at a palliative stage;
- services which are now being provided by the Society and the extent to which they meet patient and family needs;
- services which the Society is best suited to deliver;
- services which other organizations might be better suited to provide;
- services which the Society should consider initiating, expanding or withdrawing;
- changes in the provincial health care system and their potential impact on the services of the Society.

---

*Chairman, Patient Services, Canadian Cancer Society Ontario Division.

**Co-ordinator, Patient Services Programs, Canadian Cancer Society Ontario Division.

After initial consultation with physicians to ensure compliance with privacy laws, the survey was conducted via questionnaire mailed out to both patients and a family member. A small group of health-care professionals were also surveyed.

The consultants also conducted a series of focus groups and interviews and felt that the results were highly reliable and representative.

The regional distribution of respondents reflects Statistics Canada's 1986 Census Data for Ontario. The prevalence of different types of cancer among the study sample, as well as the gender breakdown, closely approximate cancer prevalence data for Canada. The report concludes "We are confident that the statistical results on key variables can be generalized to the entire Ontario cancer patient population".

Patient and Family Member Profiles

Ontario cancer patients responding to this survey came from all income levels. The vast majority were married and have children. There were slightly more females (53.6%) than males (46.4%). With respect to age, 19.3% were 50 years or younger, 37.8% were between age 51 and 65, and 42.9% were 65 years and older. This survey provided no evidence of substantial changes in patients' needs over the various lengths of time since the initial diagnosis. For 69.2% of the respondents, this was two years or less.

Of these patients, approximately two-thirds had been to a cancer clinic for consultation, treatment or follow-up. About the same number reported that they had not stayed in bed for one-half day or more in the past month. Of the 74.3%, who had received some form of treatment, this consisted of surgery (87.8%), radiation (49.9%), chemotherapy (35.3%), immunotherapy (1.3%) and other (13.5%).

Patients reported having difficulty with a variety of physical activities such as sleeping, home maintenance, housekeeping, getting around and shopping.

To pay for supplementary items needed in dealing with their illness, patients most often relied on personal savings (55%), private insurance (23.6%), and assistance from the Society (19.6%). The most common expenses were transportation to treatment (identified by 24.8% of respondents), drugs (18.3%) and supplies (13%).

More than three-quarters said they had lost employment income because of the illness. Of the 169 respondents who said their work life had

TABLE I

Distribution of Survey Population
by Ontario Region

Northern	8.4%
Southern and Central (including Metro Toronto	77.6%
Eastern	14.0%
TOTAL	100.0.%

TABLE II

Distribution of Survey Population
by Cancer Site

Breast	26.1%
Lung	4.8%
Bowel	13.1%
Prostate	12.3%
Bladder	9.4%
Mouth/tongue/oral/etc.	5.6%
Uterus, including cervix	5.4%
Ovary	1.5%

Note: All other cancer sites are represented in less than 2% of the survey population. Prevalence data were not available.

changed (31.6% of the total sample), 52.8% had stopped working entirely, 27.7% had reduced their hours, and 19.5% had changed their work.

Of the family members who responded, 75.8% were spouses, 15.5% were children, 5.5% were parents, and the remainder were siblings. In this group, there were more females (62.1%) than males (39.9%). Most of these respondents (82.5%) lived with the person who had cancer.

Major Findings and Recommendations

1. *Emotional Support.* Ontario cancer patients and their families seek support primarily from other family members, friends and physicians. While the Canadian Cancer Society Ontario Division operates 123 units throughout the province and offers a range of services, its emotional support programs are not widely used.

When asked if they would have wanted to talk to a trained Society volunteer if it had been suggested, 43% said "Yes". This suggests that these support services are not used because of a low level of awareness—rather than a lack of demand.

The consultants noted "A key element of access to service is awareness of the service", and added that another factor inhibiting use is "the social stigma often associated with having emotional problems". Of the most frequently mentioned problems, one-half related to psychosocial adjustment, e.g., "Dealing with feelings", "Accepting the presence of illness", "Maintaining intimate relationship with spouse", and "Feeling good about myself". In these areas support from a trained volunteer, who has had personal experience with cancer, could have helped.

Family members rated their own emotional adjustment as the most difficult problem. The periods of greatest emotional stress were when they first heard the diagnosis and after the patient's surgery.

Society volunteers and staff also rated emotional support as the most important need of patients. They believed it is a service which the Society is well suited to provide.

In addition to working at cancer clinics and lodges, Society volunteers offer a number of peer support services. These programs include:

Friendly Visiting	- social contact for patients
CanSurmount	- one-to-one peer support for patients, families and friends, provided by volunteers who have had cancer or have been close to someone with cancer
Living With Cancer	- support groups for patients and families
Living Cancer Education Program	- educational sessions for patients and families
Reach to Recovery	- support to patients with breast cancer

These services are not offered consistently across the province and are, in large part, unknown to patients and families.

The report recommends, therefore, that the Society strengthen the development and delivery of the peer-support services and programs that help patients and families cope emotionally and practically with cancer.

In addition, it recommends that the Society develop and implement a plan to heighten public awareness of its services in Ontario.

2. *Information.* Of all needs, over 40% of the patients and their families had information needs which were not being addressed.

   While they were generally satisfied with the information they received about medical conditions, treatment choices and side effects, they indicated a strong need for non-clinical information to help them cope with the effects of cancer, most critically in the following areas: Emotional reactions to cancer; effects on work life; effects on social life; sources of information financial effects; and services available.

   Volunteers and staff concurred with the recommendation to establish a systematic program, which develops and delivers non-clinical information tailored to the needs of cancer patients and their families. Volunteers and staff would be trained to provide this information, and that concerning other agencies and programs.

3. *Transportation.* Last year, the Society provided local transportation and long-distance travel to treatment for approximately 10,000 patients. According to the survey results, almost one-half of all patients have had to travel out of town for appointments or treatment.

   Of those who responded, 38% of patients and 79% of family members identified transportation as the most needed physical support service.

   More than 1900 volunteers drove patients to treatment last year. They also helped to arrange travel, accommodation and financial support for patients and escorts travelling long distances to treatment centres. In this setting, Society volunteers can offer information and help with daily living issues.

   The report recommends that the Society continue to provide both local and long-distance transportation services and, where possible, collaborate with other local agencies in providing these services.

4. *Financial Assistance.* Fewer than 10% of patients and family members said they needed financial help with equipment, dressings, home sup-

port, boarding allowances, ostomy supplies, prostheses or supplementary foods.

Less than 20% of respondents said that they required financial assistance with the purchase of drugs. The Society's Patient Services budget is spent primarily on transportation and financial assistance. The report recommends that the Society initiate a concerted advocacy program to encourage government to expand financial assistance to cancer patients in the areas of supplementary services.

The Ontario government is reorganizing its cancer treatment system including programs related to drug benefits, assistive devices and long-term care. The report suggests that there is now unique "window of opportunity" to advocate for the necessary financial support for these patients. The report also recommends that the Society gradually withdraw from providing financial assistance as other sources become available.

5. *Volunteers.* Generally the patient needs identified by both volunteers and staff were similar to those volunteered by cancer patients and their families. Most volunteers have worked for the Society for relatively long periods—60% have been volunteers for more than five years. It is vital that volunteers have the training to deliver such assistance as peer support and non-clinical information.

   The report recommends that the Society expand its training program for volunteers and expand the volunteer recruitment program. Society units located near regional cancer centres face heavy workloads. Thus the report recognizes the need for staff support to these volunteers.

6. *Service Collaboration.* The Ontario government hopes to encourage more collaboration in the planning and delivery of health care in order to conserve resources and provide better co-ordination. Moreover, the trends toward a decentralized health care system and expanded community-based services are likely to place greater demands on the voluntary sector. For these reasons, the report recommends that the Society collaborate with other agencies and associations in areas such as joint recruitment and training of volunteers, advocacy coalitions and shared delivery programs.

7. *Other Recommendations.* Because government policy puts emphasis on quality assurance and health-care innovation, the report recommends that the Society develop and implement methods of assessing service

effectiveness, and that a portion of the patient service budget be allocated to providing support for new service innovation.

The remaining recommendations are:

- work with ethno-cultural agencies to enable them to provide services to cancer patients in their communities
- define the range of services which, ideally, could be offered and ensure that the minimum level is available through each unit
- develop a mandate statement for patient services
- establish a plan to implement the recommendations of the study.

Conclusion

The report has been approved by the Board of Directors, and its implementation is being undertaken by the Canadian Cancer Society Ontario Division. Volunteers and staff of the Society in all parts of the province are being closely consulted throughout this process.

For a copy of the report, please contact the Canadian Cancer Society Ontario Division, 1639 Yonge Street, Toronto, Ontario M4T 2W6 (tel. 416-488-5400).

Studies of patient needs also have been conducted in Prince Edward Island, Manitoba and Quebec. For further information, please contact the Canadian Cancer Society's national office, 10 Alcorn Ave., Ste. 200, Toronto, Ontario M4V 3B1 (tel. 416-961-7223).

CANCER 2000: BUILDING A UNITED COMMUNITY

Wm.K. ADAIR, B.S.W.* and M.I. FITCH, Ph.D.**
Toronto, Ontario

Those who work in cancer control face unparalleled challenges and opportunities. In 1990, approximately 104,000 people in Canada were diagnosed with cancer for the first time and approximately 54,500 people died from this disease[1]. It has been estimated that, between 1988 and 1994, the number of new cases of Cancer in Ontario alone will rise from 38,263 to 48,000[2]. By the year 2001, an aging population and immigration will produce almost 60,000 newly diagnosed cancer cases in Ontario, leading to a 50% increase in 10 years[3]. While cancer is the second leading cause of death in Canada, the direct costs of treatment in 1986 (1.9 billion dollars) ranked seventh in relation to other direct health-care expenditures[4]. Competition for health-care dollars is fierce while government funds available for services are shrinking[5]. Patients, once passive recipients, are becoming aggressive consumers, who demand equal access to quality care[6]. The increasingly complex network of health care professionals is finding great difficulty in meeting the demand for services that are technologically advanced yet delivered in a humane manner.

In Canada, a large force of dedicated people work hard day by day to save lives and reduce human suffering caused by cancer. Recognizing the benefits of co-ordinating independent efforts into a united community, leaders in cancer control formed a two-year task force entitled Cancer 2000: Strategies for Cancer Control in Canada. The goal of Cancer 2000 is to develop a framework for the co-ordination of cancer control in Canada[7].

History

Cancer 2000 grew out of a 1988 conference entitled "Cancer Control in Canada: The Challenge to Coordinate". This conference was convened to plan for better co-ordination within the cancer control movement in Canada and to identify the most appropriate framework to facilitate such co-ordination.

---

* Director, Cancer 2000: Strategies for Cancer Control in Canada, Toronto, Ontario.

** Oncology Nurse Researcher, OCTRF, Toronto-Bayview Regional Cancer Centre.

At the conference more than 80 delegates from both provincial and national cancer agencies and health-related organizations engaged in a frank debate concerning problems related to co-ordination. The first day provided an analysis of co-ordination in Canada and looked at how cancer agencies in Canada and around the world achieved co-ordination. The delegates gave unanimous consent to a motion to support further investigation. On the second day, delegates formed a national task force to work for improved co-ordination of cancer prevention and control efforts in Canada. A steering committee established the general terms of reference for this task force, appointed members, and applied for required funding.

On September 30, 1989, the then Federal Health Minister, Perrin Beatty, announced a grant of $492,451. The Canadian Cancer Society and the National Cancer Institute of Canada committed themselves to contribute the balance.

Process

The task force has provided key stakeholders across Canada with an opportunity, collectively, to examine problems and develop a cooperative approach to our common goals.

> "Self-examination is the key to insight which is the key to wisdom."[8]

The formula for success of the Cancer 2000 task force has been simple: we believe that those people intimately involved in designing and managing cancer control programs throughout Canada are in the best position to describe existing problems and to work together to create successful solutions. Based on this principle, we designed a process for continuing input from all stakeholders involved in cancer control. In addition to a general call for input, we identified a number of essential players:

- Cancer patients/families
- Provincial/Federal governments
- National organizations
- Provincial work groups
- Expert panels
- Colleagues in other countries
- Ethnic communities

Key leaders in each province and territory formed a Provincial/Territorial Work Group (PWG) to provide input to the task force. They were asked to advise about strategies for the co-ordination of effective cancer control activities in their province/territory and the rest of Canada. More than 300 national organizations were invited to make a written submission and nine expert panels were formed to examine specific areas.

The task force has worked in two stages: The first, which concentrated on input from the stakeholders, concluded in December 1990. The second, engages the stakeholders in a co-operative exchange to produce and revise recommendations for the final conference in October 1991.

Ontario Provincial Work Group

The Ontario Ministry of Health, the Canadian Cancer Society Ontario Division, and the Ontario Cancer Treatment and Research Foundation believed it was essential to be part of the Cancer 2000 process. In a joint effort, they formed the Ontario Provincial Work Group (OPWG). They accepted responsibility to provide input to the Cancer 2000 task force and to engage in dialogue at the national level, however they also wished the gathering of information about the co-ordination of cancer care, and the generation of recommendations, to benefit Ontario. The OPWG appointed Dr. Margaret Fitch as Chairperson in March 1990, and selected eight provincial work group members representing the membership of healthcare professionals, cancer patients and volunteers. The work group held its first meeting in April, 1990.

Initially the group gathered information about cancer control and its co-ordination in the province. Because the number of individuals, agencies and institutions involved in cancer control was increasing steadily, the group sought a broad outreach to capture a range of perspectives on cancer control co-ordination. In data gathering, they used many approaches and checked a wide number of sources. Due to the short time available, data gathering focused on areas on which we had little or no information. Where possible the work group used existing reports and documents. They sent invitations or questionnaires to:

- Provincial professional associations
- Provincial associations with a health-related mandate
- Educational institutions/agencies
- Service or care providers
- Hospice, palliative care and self-help groups
- Experts in various fields of cancer control

The group's approach encouraged multidisciplinary input and incorporated a patient focus, which are reflected in the range of data we have received.

The work group sought to identify patterns and trends within the response data in order to identify common themes and key issues. The work group will base its future activities on these key issues. Many have written to express their excitement about the process of Cancer 2000; they believe this work is important. Many asserted that it will make a real contribution to future cancer control in Ontario.

Products of Cancer 2000

Cancer 2000 task force will conclude by providing two main products.

First, they will propose a framework for co-ordination. This structure will help all "players" to work together as they apply human and financial resources to reduce the incidence, morbidity, mortality and suffering caused by cancer. Our model will make recommendations concerning the implementation of specific strategies at the provincial, territorial, national and international levels. This plan will be presented for evaluation and ratification to a national conference in November, 1991.

The second product is information. We will describe accurately the status of cancer control activities in Canada, with a particular emphasis on key issues and/or impediments to cancer control. This inventory will be more extensive and thorough than anything heretofore available. We hope to generate recommendations for action from this accumulated knowledge base. Provincial/territorial work groups, national organizations and expert panels all will contribute substantially to the information pool and to the proposals which will flow from it.

Even though much will have been accomplished at the end of the task force's two-year mandate, this is only the beginning of a process, which must become self-perpetuating and self-validating. The striving for improvement must continue in all sectors across the entire land.

As information supports the development of structure, and structure creates a demand for more information, a dialectic of change will be born. Our long-term goal will be realized only when widespread harmony and processes of improvement become commonplace within our cancer-care community.

REFERENCES

1. National Cancer Institute of Canada. *Canadian Cancer Statistics 1990*. Toronto, Canada, 1990. p.9 (Table 1).
2. Ontario Cancer Registry. Personal Communication.
3. NCIC Advisory Committee on Cancer Control. *Discussion Paper on Cancer Control in Canada*. Toronto, Ontario. June 28, 1990, p.4.
4. *NCIC Canadian Cancer Statistics 1990*, p.59.
5. *The Globe and Mail*. "Tories Hurting Medicare, Abandoning Jobless, Critics say." February 28, 1991. p. A6.
6. *Cancer 2000: Strategies for Cancer Control in Canada*. "Report of the Expert Panel on Patient Needs." January 14, 1991.
7. Cancer 2000: Strategies for Cancer Control in Canada. *The Networker* (No. 1/Winter 1989/1990), p. 3.
8. Peck MS: The Different Drum: Community Making and Peace. Toronto: Simon & Schuster Inc., 1987: 66.

INEQUALITIES IN CANCER CONTROL IN CANADA

J. C. Laidlaw, M.D.*, *Toronto, Ontario*

"Of all the forms of inequality,
injustice in health is the most shocking
and inhumane."
- Martin Luther King

Factors such as socioeconomic status, education, place of living, gender, age, mental or physical handicap, and ethnocultural background, as well as one's genes have been shown to produce inequalities in many areas of health. In 1990, the Cancer 2000's Panel on Cancer and the Disadvantaged carried out a study to determine whether these factors produce inequalities in cancer control in Canada** and submitted it to the Cancer 2000 Task Force. Cancer control is said to involve the following components: prevention, early detection, diagnosis, treatment, rehabilitation and palliative care. Treatment and palliation involve the care of the patient and her/his family as well as care of the disease. Strategies for improving cancer control include research, legislation and education of both the public and health professionals.

In the time available, the Panel found it possible to study only the influence of socioeconomic status, ethnocultural background (with emphasis on Aboriginal peoples), gender (women) and age (the elderly) on the following components of cancer control: prevention, early detection, diagnosis and treatment.

Their principal finding was that we have very little information concerning inequalities in health care in general and inequalities in cancer control in particular in Canada. What information is available points to major inequities in the areas studied and notes that frequently a combination of the "disadvantage" factors are responsible for the inequities in particular sectors of our population e.g. in Aboriginal peoples and in the elderly.

---

*Director, Research and Education, and Vice-President, OCTRF; and Executive Director Medical Affairs, Canadian Cancer Society, National Office, Toronto, Ontario.

**The members of this Panel were as follows: Lorna Cooper, B.Sc.N.; Suzanne Desaulniers, M.Sc.; John Maher, M.A.; Ralph Masi, M.D.; Joan Milling, M.A.; Don Wigle, M.D.; Kathryn Wilkins, M.Sc.; John C. Laidlaw, M.D. Copies of this study can be obtained from Dr. J. C. Laidlaw, Canadian Cancer Society, 10 Alcorn Avenue, Toronto, Ontario, M4B 3V1

The study made the following major recommendations:

1. There is an urgent need for more extensive and ongoing study of inequalities in health in general and inequalities in cancer control in particular in Canada.

2. There is a need for research on those genetic and environmental factors which may be responsible for the increased incidence of certain cancers in certain sectors of the Canadian population.

3. Particular sectors of the Canadian population, e.g. the poor, ethnocultural communities, women and the elderly, should be represented in all stages of the development, implementation and operation of cancer control programs.

4. Further study is required of the needs of those who are disadvantaged with respect to the components of cancer control.

5. Information about cancer control programs must be tailored to the groups for which it is intended. For each group the information must be presented in a sensitive manner, with a message that is understandable and practical and delivered through a medium that is accessible. This recommendation applies particularly to disadvantaged sectors of the population.

6. Research is required on the development of effective measures for the control of cancer-producing lifestyle factors in disadvantaged sectors of the population.

7. Research is required on the barriers to access to cancer control programs experienced by disadvantaged groups. Research is also required on the means to overcome these barriers.

8. Health professionals must be educated at the undergraduate, postgraduate and continuing education levels in care in general, and in cancer control in particular, for disadvantaged sectors of the population.

RESEARCH ON CLINICAL DECISION MAKING AND HEALTH-RELATED BEHAVIOR

J.E. TILL, Ph.D.* and H.J. SUTHERLAND, R.N.**
Toronto, Ontario

1. *Clinical Decision Making in Oncology*. Underlying many, if not all, clinical decisions are judgments about the value of life in different states of health. Our early work on clinical decision-making involved the measurement of patients' utilities or values for health states. This led to a particular interest in decision-making from the patient's perspective, and, in particular, in developing ways to help patients to participate in decisions about their own care. For example, we examined cancer patients' desire for information and participation in treatment decisions regarding standard therapy and found that patients do actively seek information, but are uncertain how to use such information. These findings have, in turn led to explorations about the understanding patients have of information. One of our current research projects is concerned with the relevance of such information to decisions patients make regarding entry into randomized controlled clinical trials.

2. *The Randomized Controlled Trial (RCT) as a Model Within Which to Study Patients' Decision Making*. RCTs stand at the interface between fundamental science and its application to human disease. Since scientific, legal, and ethical considerations all must be addressed, RCTs are an obvious and interesting situation within which to examine patients' decision-making processes. As outlined in Section 3 below, we are interested in the RCT as a well-defined context within which to examine a particular type of health-related behavior. However, our choice of this model also was motivated by two important practical considerations: the ethical incentive for informed decision-making on the part of patients, and the medical and scientific incentive to evaluate therapies using rigorous RCTs.

A crucial pre-requisite for a successful RCT is the accrual of sufficient numbers of patients. However, recruitment difficulties have plagued a number of cancer trials. Some attempts have been made to explore the perceptions of physicians concerning the entry of patients into cancer trials. We examined reasons why patients are (or are not) offered entry into RCTs and found differences in the perspectives of oncologists, nurses and family physicians. The latter two groups gave less emphasis to scientific considerations than the oncologists and assigned more importance to the doctor-patient relationship. This study did not seek the perspective of patients on these factors; indeed, little has been done to investigate the reasons why patients agree or decline to participate. A few reports have appeared regarding patients attitudes and public opinion in non-cancer trials and cancer trials. More recently, we have taken the view that patients' perspectives are of utmost importance in the decision to enter RCTs, and have completed two studies. Both investigated patients' perceptions of information appearing on a consent form. Consent forms are an excellent model of the kind of information being provided to patients offered entry into RCTs and thus are suitable for experimental manipulation. We focused our initial attention on the information in the consent form, to the exclusion of other possible influences, such as the patient's perception of the pressure that others, e.g. health professionals, family and friends, put on the individual to consent (or not consent) to enter a trial. We will begin to explore such influences in a study currently being planned (see Section 3).

---

*Senior Scientist, Division of Epidemiology and Statistics, Ontario Cancer Institute, Toronto; and Professor of Medical Biophysics, University of Toronto.

**Research Associate, Division of Epidemiology and Statistics, OCI.

Our first study of patients' perceptions concerning information in a consent form elicited numerical interpretations for individual verbal descriptors of probability, which appear on consent forms in our institutions. For example, these use words such as "rare", "frequently", "occasionally", etc. to indicate the likelihood for certain benefits and risks. We asked 100 patients with cancer to give a number, in the form of a percentage, to represent their interpretation of each probabilistic word or word-phrase. We concluded that, within this group of patients, there was no consensus about the numerical meaning of a given word. Since others have demonstrated the same phenomenon in health professionals, there appears to be a great deal of "noise" in this particular line of communication. Thus, the beliefs subjects hold about the meaning of probabilistic information may have a major influence on decisions about participating in a trial, and these interpretations may be quite independent of the information which the health-care team (who also have their own belief systems) intended to convey. The patient who believes "rare" indicates a 15% chance of some event may make a different decision than one who assigns a 1% probability to the likelihood of a "rare" event.

Probabilistic terms are but one type of information contained in a consent form. Our second study examined the relevance to, and use made by patients of, all the information appearing on a consent form, which described a hypothetical RCT. We asked patients to indicate which aspects of this information would influence (positively or negatively) their decision about whether to enter the hypothetical RCT. This study also examined their interpretations of certain pieces of information involving probability statements related to the trial, including the meaning of randomization. In addition to not weighing the pros and cons of the trial, many patients did not interpret correctly the probability statements, especially the meaning of randomization. This finding is particularly disturbing. Using the same trial description, we now propose to investigate systematically the attitudes and beliefs which determine participation.

3. *Predicting Health-Related Behavior*. Many are showing an increasing interest in understanding and predicting health-related behavior, chronic illness behavior, etc. Generally, in patients with cancer, one is interested in chronic illness behaviors, which are said to be those aimed at reducing risk of further illness and maintaining health.

The theory of reasoned action (TRA), a well-known conceptual model, has been proposed to predict and understand health-related behavior. The TRA has been used in studies of health-related behaviors, especially smoking, dieting and exercise and others, such as consumer behavior, voting behavior, and women's occupational orientation. In a search using MEDLINE, we found about 100 publication titles relating to the theory but came across no applications to clinical-trial participation. Although the TRA seems to be more useful for studies of some behaviors than others, it appears to be the most promising framework within which to explore the relationship between behavior, attitudes and beliefs. We propose to use it to investigate factors which influence cancer patients' intentions to enter randomized clinical trials.

4. *A Multidisciplinary Challenge*. This note has outlined the evolution of our research program, beginning with work on clinical decision-making involving the measurement of patients' utilities or values of health states. Quality-of-life assessment led us into studies of decision-making from the patient's perspective, and then, recently, into studies of health-related behavior. The evolution of our research provides one illustration of the broad range of issues which need to be approached using rigorous and quantitative research methodologies drawn from such disciplines as epi-

demiology, biostatistics, and the behavioral and social sciences. This dependence on several scientific disciplines is analogous to the dependence of research in tumor biology on several biological sciences. Investigators interested in the broad range of issues outlined here are challenged to attain a level of expertise in a set of disciplines, which is even more diverse than the set which tumor biologists must confront.

References are available upon request from:
Dr. J.E. Till
Division of Epidemiology and Statistics
Ontario Cancer Institute
500 Sherbourne St.
Toronto, Ontario
M4X 1K9

BEHAVIOURAL RESEARCH AND CANCER

P.G. SCHOLEFIELD, Ph.D.*, *Toronto, Ontario*

The ultimate objective of most individuals and agencies concerned with cancer is to reduce the incidence, morbidity (including suffering) and mortality from the disease. Over the years pursuit of this objective has led to many contributions to cancer treatment and cancer research based primarily on medical and biological approaches. However, more recently, many have shown interest in a third approach "cancer control", a concept which conveys separate meanings to different individuals and agencies. Cancer control research includes studies of such diverse areas as health promotion, psychosocial aspects of cancer and population health. Table I shows the relationship between some of the classical discipline-oriented divisions of cancer research and their three distinct but interdependent streams. Many of the items in these three streams are concerned with human behaviour and the attitudes and beliefs which modify it. This paper will illustrate this relationship by focusing on the public, the professionals, the patients and the politicians.

Often the public seems to demand that its agents direct more resources to the prevention of cancer but seems reluctant to act upon recommendations designed to reduce these risks. Cases in point are the mounting deaths from lung cancer caused by human smoking behaviour, the occurrence among the minority of women, who have never had a Pap test of the majority of deaths from carcinoma of the cervix, apathy concerning the emerging advice on the relationship between diet and cancer etc. On the other hand, the public in Canada and elsewhere continue to contribute time and money to organizations such as the Canadian Cancer Society. Can we improve our performance by studying this important area of human behaviour?

When we are estimating the impact of cancer in the 20th and 21st centuries, we must consider the behaviour of professionals to be a major determinant. In their training programs, health professionals are given little or no guidance on communication, yet it is generally accepted that the family doctor is able to make a major contribution to health-oriented decision making. Specialist and nurses have the ultimate responsibility for explaining to patients and families all the implications of the disease and its treatment but even they receive no professional training for this important task. Of course, professionals need special training and experience for palliative care and pain control.

---

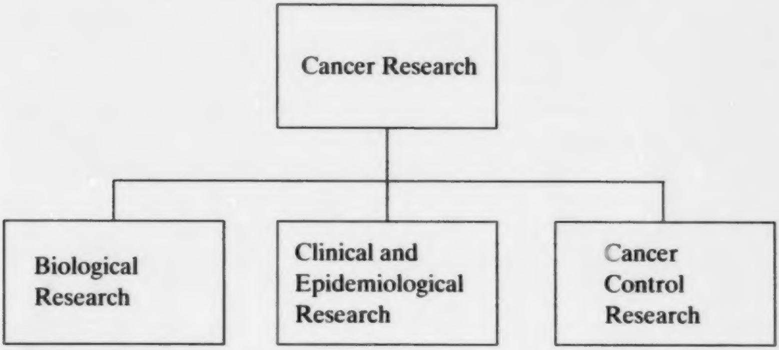
*Executive Director, National Cancer Institute of Canada.

We are devoting increased attention to the behaviour of patients and their immediate family in coping with a diagnosis of cancer, in understanding current approaches to treatment and in dealing with the terminal phase of cancer. As new diagnoses of cancer increase so will the need for these services and the evaluation of their effectiveness. Similarly patients are becoming more involved in making decisions about treatment; this movement will require an analysis of the basis on which such decisions are made and on whether patients agree to accept standard treatment or to enter clinical trials.

The behaviour of politicians has a great influence on cancer control because this group has the ultimate responsibility for setting priorities. They determine public approaches to legislation on tobacco advertising, the control of environmental carcinogens, the funding of medical services, the training of professionals, the initiation of screening programs, the support of research facilities etc. These men and women face great challenges, the consequences are critical and we must learn more about the processes involved and the factors which influence them.

Who should undertake behavioural research? Most types of research should be undertaken by well-qualified individuals to ensure that the results will stand up to the usual process of peer review. Unfortunately many of those who are qualified are not interested and many of those who are interested are not qualified. Our first objective here should be to persuade qualified individuals to become interested in behaviour and cancer. This will require government allocation—perhaps reallocation—of resources and a public commitment to support psychologists, social scientists and other professionals and provide adequate research opportunities similar to those available for medical and biological research. Our second goal should be to make it possible for interested individuals to obtain the necessary research training. For example, nurses provide care 24 hours a day so they are in an ideal position to contribute to all aspects of research involving the needs of cancer patients. Presently the nurses' professional training does not prepare them for research careers and nurses should be given more opportunities for training up to the Ph.D. level. Similarly, only a handful of medical specialists have training that qualify them to undertake research into the psychosocial needs of cancer patients; thus a new cadre will emerge only if we create new opportunities for training and careers.

TABLE I
Discipline-Oriented Divisions of Cancer Research



Biological Research	Clinical and Epidemiological Research	Cancer Control Research
Virology	Clinical Trials	Health Promotion
Physics	Epidemiology	Psychosocial
Immunology	Human Subjects	Evaluative
Cell Biology		Outcome Research
Genetics		Data Development
Biochemistry		Population Health
Carcinogenesis		Rehabilitation
Pathology		Policy Research
		Social Marketing

Where should behavioural research be conducted? Many opportunities exist within continuing medical education programs, in several recently created health promotion centres, in departments of behavioural science, psychology, social work, psychiatry, ethics etc. and in research institutes. Unique opportunities, involving patients and their families, exist in specialized cancer clinics and in the teaching hospitals for research. The programs of the Canadian Cancer Society provide an ideal environment for the study of the needs, development, evaluation and delivery of nationwide programs. Federal and provincial government programs are ideal locations for demonstration projects and form the essential link joining "the ivory tower" to the frontiers of program delivery. In short, opportunities abound.

Who should support research relating behaviour to cancer? Certainly agencies such as the Medical Research Council of Canada, the National Cancer Institute of Canada, the National Health Research and Development Program and the Social Sciences and Humanities Research Council should continue to provide support. However, they must ask whether their allocations adequately match the available opportunities. Other provincial agencies and those participating in health-oriented programs might, on the basis of the results of program evaluation, decide how to re-direct their resources and determine how best to effect behavioural change. Insurance companies and other business enterprises, which depend on a healthy public, would do well to consider an investment in behavioural research.

Finally, we need to consider the national and international aspects of behaviour and cancer. Culture will be a major factor when we attempt to modify behaviour related to cancer. Canada, a land of many cultures, is challenged to devise a national program which would change behaviour despite this mix of cultures. Will the fisherman from Newfoundland respond in the same way as the city dweller in Quebec or the prairie farmer? Will the behaviour of our immigrants from Eastern Europe, India, the West Indies and Viet Nam respond to the same interventions in the same way? Can we adapt the results in other countries to meet Canadian needs? Can the Canadian success in influencing legislation on tobacco be adapted to prevent multinationals from seducing the developing nations? What role should Canadian government and voluntary health grant agencies play in helping other nations, especially developing nations, cope with their problems relating human behaviour to human cancer? We have learned much from our colleagues in Australia, Europe and the United States. We are learning more about ourselves through ventures such as Cancer 2000, which have aroused a great deal of interest in Canada. Now is the time for us to decide that we have been presented with a tremendous opportunity.

HELPING PATIENTS COPE WITH AND COMBAT CANCER

A.J. CUNNINGHAM, Ph.D., C.Psych.**,
Toronto, Ontario

For the last nine years, at the Ontario Cancer Institute/Princess Margaret Hospital, we have conducted a series of programs for cancer patients called "coping skills training". These classes provide emotional support, along with instruction in a variety of self-help techniques: deep relaxation, positive mental affirmations and imagery, lifestyle changes, meditation, journal keeping, writing a life history and others, most of them in wide use in psychology. Detailed evaluation of the programs shows that they substantially improve the quality of life of most participants, changes being noted in mood, interactions with other people, some physical symptoms, and sense of control over events. An analysis of data for some 400 patients over five years has shown that benefits are similar for people of different marital status, religion, education level, diagnostic site and stage of disease, and gender, while younger patients (less than 50 years) appear to profit more than do older peoeple. A randomized control comparison has demonstrated that coping skills training produces more improvement than simply meeting and discussing problems. The Canadian Cancer Society now distributes our basic, six-session program across Canada as a booklet and audiotape set under the title: "Helping Yourself".

Our current studies include efforts to extend and better understand the effects of training in coping skills on quality of life. For example, a randomized trial is underway comparing the effects of delivering the standard program as as six weekly sessions or as a "weekend intensive". However, attention is now shifting to the more controversial and more interesting question as to whether psychological help can ifluence length of life[1]. Several lines of evidence point to an impact of mental state on cancer itself: experiments with animals, showing a relationship between stress and cancer growth; studies on the personality of cancer patients, suggesting a relationship between emotional repression and poorer prognosis; and clinical trials of the impact of psychosocial therapy on longevity. In this last category there are two published randomized trials, both with metastatic breast patients: one claims a 6-month prolongation of life in women receiving individual psychotherapy[2]; and one showing a remarkable 18 months' average increase in lifespan for women who attanded a support group once a week for a year[3]. While the former study has been criticized, experts in the clinical trials field seem to agree that the latter is methodologically sound, although small (86 patients in all). Obviously it is important to replicate and extend these studies. We are engaged in a pilot trial with metastatic breast cancer patients, which will undertake to do this and to gather further information about the kinds of cancer which correlate with long survival. Such a research project is difficult because the subjects must be sufficiently motivated to attend support groups and practise self-help techniques over a long period (and relatively few are), yet they can be offered only a 50/50 chance of the psychosocial help. The main stumbling block so far is the accrual of sufficient patients.

---

*Senior Scientist and Clinical Psychologist, Ontario Cancer Institute/Princess Margaret Hospital; and Professor of Medical Biophysics, University of Toronto.

What are the implications of this work for cancer patients in the future? From our own data, and the results of others, it seems clear that quality of life can be improved by simple, cost-effective, group interventions. Whether such programs will be added to regular cancer treatment seems to depend more on an adjustment of health-care priorities than on any need for further scientific justification. We require a shift away from the purely "crisis" approach of offering psychological support only to those who exhibit significant distress, towards a recognition that cancer poses a series of novel and progressive problems for which most patients have inadequate coping skills. Concerning the question of whether life can be prolonged by psychosocial help, although this is not conclusively proven, there is evidence to suggest that it is a strong possibility: further research progress will depend on availability of funding and an open-minded attitude on the part of oncologists and other cancer scientists.

REFERENCES

1. Cunningham AJ: The influence of mind on cancer. *Can Psychol* 1985; **26:** 13.
2. Grossarth-Maticek R, Schmidt P, Vetter H, Arndt S: Psychotherapy research in oncology. *In:* Steptoe A, Mathews A, eds. Health Care and Human Behaviour. New York: Academic Press, 1984: 325.
3. Spiegel D, Bloom JR, Kraemer HC, Gottleib E: Effect of psychosocial treatment on survival of patients with metastatic breast cancer. *Lancet* 1989; **14:** 888.

PALLIATIVE CARE AND THE CONTROL OF SUFFERING

J.F. SCOTT, M.D.*, *Ottawa, Ontario*

In Ontario over 50% of cancer patients die of their disease after months or years of suffering characterized by fluctuating levels of pain, other symptoms and psychosocial distress. Yet, the health-care system has focused little attention on these patients and their families and has not studied the mechanism and modem management of these symptoms. Palliative care services in Ontario, lack adequate funding and seldom are co-ordinated with the services of the Ontario Cancer Treatment and Research Foundation (OCTRF). However, we are now witnessing a radical shift in the government attitude, a shift spurred by consumerism, economic pressure and academic opportunity. Cancer patients are demanding increased access to information and a larger role in decision-making including the decision to live and to die with cancer in their own way and in their own place. They are urging us, not only to cure and prolong life, but to relieve their pain and control their suffering. Increasingly, governments are recognizing that in order to control spiralling health costs, they must support palliative care in order to set limits on inappropriate and expensive investigations and therapy in the last months of life. Increasingly the academic cancer community has become disillusioned by the poor results of research in molecular biology and chemotherapy trials and has turned, with growing excitement, to research into symptoms and suffering—a virgin area where results can be applied immediately at the bedside.

Burden of Suffering

In Ontario in 1988, 18,806 persons died from cancer. If mortality rises at the same rate as incidence (over 3% per year) we can expect more than 25,000 deaths annually by the year 2000. Although Ontario collects excellent disease-focused data, we have little information on the quantity, scope or length of suffering in cancer patients. As cancer becomes a semi-chronic illness, we are encountering an increasing demand for a complex range of palliative-care services. As better treatment lengthens survival in those with metastatic disease and lung primaries, these patients will require palliative care for longer periods. We are facing more difficult symptom-complexes including a rapid increase in the incidence of neuropathic pain syndromes. Also new resources are needed with the aging of the population and the co-presence of multiple chronic illnesses. The delivery of such care is further complicated by rapid changes in family and community-support systems, e.g., aging of the family caregiver, increasing proportion of population in the work force and smaller, mobile and fragile families. In summary, by the year 2000 Ontario will face a staggering increase in the burden of cancer suffering.

---

* Director, Regional Palliative Care Service; and Head, Palliative Medicine, University of Ottawa.

Definition

In 1989, Health and Welfare Canada adopted the following definition:

> "Palliative Care is a program of active, compassionate care primarily directed towards improving quality of life for the dying. It is delivered by an interdisciplinary team that provides sensitive and skilled care to meet the physical, psycho-social and spiritual needs of both the patient and the family. The philosophy and principles of Palliative Care may apply to patient populations other than the dying and Palliative Care Program may have a secondary role in addressing the needs of these groups."[1]

The true definition of palliative care continues to generate major controversy within the cancer community. Many centres object that its apparent focus on death excludes patients in the earlier stages, who require symptom control and psychosocial support. However the development of postgraduate programs in palliative medicine throughout the world and expanding research into the management of symptoms and suffering in advanced disease, has led to growing acceptance of the concept of palliative medicine or palliative oncology as an integral part of a cancer treatment and research foundation. Within such a centre, palliative medicine participates in symptom control and psychosocial support regardless of prognosis but with a clear weighting towards those with advanced disease. By offering an active, effective and academically challenging alternative to disease-oriented treatment, consultants in palliative medicine assist their colleagues in medical and radiation oncology to choose their therapies more judiciously and thereby prevent frantic, costly and ineffective attempts to prolong life.

Inventory of Programs

In the last decade three surveys have been done to monitor the development of palliative care—in 1981 and 1986 by the Palliative Care Foundation and in 1990 by the McGill Palliative Care Service[2]. The years 1981 to 1986 saw a rapid growth in palliative care programs in Ontario but since 1986 this development has come almost to a complete halt (Table I). There has been limited growth in community-based programs but a decrease in hospital-based programs. However the number of hospital-based programs that have palliative care beds has increased slightly. It is important, however, that approximately 60% of these 291 beds were scattered throughout the hospital. These "scattered beds" appear to represent administrative estimates of the number of beds presently occupied by dying patients and should not be viewed as distinct programs of palliative care. In the Fall of 1990, a survey of palliative care programs by the Ontario Ministry of Health documented 157 palliative care beds in chronic care hospitals, and 77 general hospitals reporting consultation programs staffed by a total of 47 professionals—most of whom were nurses[3].

The Ontario Palliative Care Association, which is affiliated with the Ontario Hospital Association, represents all health-care professionals involved in palliative care. At present it is working with national and provincial bodies to develop accreditation criteria and standards of care. The Ontario Medical Association has a section on palliative care and, within it, over 250 physicians have committed themselves to the advancement of this new discipline through education and tariff reform. All five Ontario Faculties of Medicine have begun to develop undergraduate and postgraduate training programs in palliative care.

At present, the OCTRF has no policy on palliative care and does not document palliative care activities within the regional cancer centres. Individual centres have experimented with a variety of models, some focusing on the management of late-stage disease while other provide earlier supportive care. Some centres have developed interdisciplinary psychosocial support teams while others have focused on symptom-control narcotic- infusion programs. Global budgets have been squeezed to hire additional personnel and to develop specialized outpatient clinics and inpatient consultation teams. Yet, at the moment, most regional centres are struggling to develop a philosophy of care and are searching for a delivery model.

Fourth Phase of Cancer Control

The World Health Organization urges governments and cancer centres to control cancer in a four-part strategy: prevention, early detection, treatment and palliative care. In January 1991, the Expert Panel on Palliative Care for the Cancer 2000 Task Force called for a re-ordering of priorities so that palliative care and control of suffering would be viewed as an essential fourth phase within Canada[4]. The report recommended:

- –A radical shift in the allocation of cancer resources so that the control of suffering receives a just and equitable share.
- –A detailed measurement of the burden of suffering and the effectiveness of palliative care in relieving this burden.
- –A major shift of resources into home care, including government reimbursement to the family for lost income and expenses while providing home care.
- –Accreditation of cancer centres based on the ability to relieve pain and provide palliative care.
- –The development of regional palliative care centres closely associated with regional cancer centres to act as teaching, research and consultation units for an entire health region.
- –The development of a Division of Palliative Oncology within every regional cancer centre.
- –Restriction in therapies and investigations, which have little proved benefit, and shifting these funds to pain relief and palliative care.
- –National Cancer Institute of Canada take a proactive stance towards palliative care research.

Economics and Health Policy

Can we afford palliative care? Faced with trade-offs and rationalization of scarce resources, how can the Ontario health system fund the recommendations of the Cancer 2000 Expert Panel? Those who ask the question in this form assume that palliative care represents a "set of frills" to be added to the "essential" components of cancer treatment. Instead, governments and cancer centres must recognize the tremendous potential of palliation to increase the quality while decreasing the cost of care. Palliative care is a philosophy and a set of resources, which can decrease cost by:

a) Cost-effective use of cancer investigations, e.g., limiting the search for a primary in the presence of an unknown primary and limiting investigations in metastatic disease when the results will not change therapy.

b) Discouraging relatively ineffective cancer therapies offered at huge cost to the patient and health-care system by asking questions about the goals of treatment, by ensuring informed consent and by providing an active alternative approach in advanced disease.

c) Decrease the practice of routine follow-up visits to cancer centres by shifting the management of palliative care patients into the community and to the family physician.

d) A regional system of palliative care can decrease length of hospital stay for cancer patients, decrease the rate of hospitalization and eventually decrease the number of beds required.

e) Palliative care encourages tertiary prevention through the identification of risk groups so that by early management of symptoms and psychosocial problems later complications are prevented or reduced.

The Ontario Ministry of Health has never developed a palliative care policy despite the promises of three governments, repeated over more than a decade. In July 1990, Cabinet approved a policy on palliative care, which included a mechanism for considering proposals for service co-ordination and education. However, this initiative, which was never announced to the public, is now under review by a new government.

Palliative care is an exciting dimension of cancer treatment and cancer research but it is in urgent need of planning and funding. The development of strong, academic and clinical programs of palliative medicine within OCTRF centres, offers a great challenge and opportunity to the Ontario cancer control system. We must spare cancer patients unnecessary suffering by accepting this challenge without delay.

REFERENCES

1. Health and Welfare Canada, Palliative Care Services Guidelines, 1989. Cat. No. H39-32/1989 E.
2. Cummings-Ajemian I: Palliative Care in Canada. 1990. *J Palliat Care* 1990; 6: 47.
3. Ontario Ministry of Health, PROVIDING PALLIATIVE CARE—A Review of the Current Status in Ontario, December 1990.
4. Expert Panel on Palliative Care, Cancer 2000 Task Force; December 1990. (Personal Communication)

Table I

PALLIATIVE CARE IN ONTARIO*

	1981	1986	1990
Total Programs	54	143	143
Programs with both Hospital & Community Components	–	–	42
Community Programs	–	–	44
Hospital Programs	–	–	57
Hospital with Beds	–	23	28
Number of Beds	–	252	291

*Cummings-Ajemian 1990

MEANING OF PAIN IN CANCER

C. DAVIS, Ph.D.*, *Toronto, Ontario*

Many cancer patients have significant pain, especially in the terminal stages of their illness. The Toronto-Bayview Regional Cancer Centre has developed a multidisciplinary pain team, which provides consultation to patients of the Centre and to outside referrals. This team, headed by Dr. Ian Kerr, includes oncology physicians (Dr. H. Dawson and oncology residents), nursing co-ordinators (Ms. M. Sone and Ms. S. Burlein-Hall), a pharmacist (Dr. C. De Angelis), and a psychologist (myself or Dr. B. Doan). All members of the team see patients at a weekly outpatient clinic, and make treatment decisions with input from all team members, including the patient. Over the four years of the clinic's operation we have worked together to provide psychological assessment and intervention in a clinic setting, where contact with the individual patient may be brief and infrequent. This paper will not offer a comprehensive summary of the psychological disturbances that patients bring to the pain clinic, but will describe our evolving clinical approach and some of the interventions we have found helpful in our work with cancer pain patients. Although I will stress the psychologist's role in the clinic, the reader should remember that this is a team activity and that each member makes a contribution to a better understanding and to the maximum alleviation of all aspects of the patient's suffering. In the same regard, this paper will not discuss such typical functions of the psychologist as assessment of clinical depression, extreme anxiety, or substance abuse. Although these are important and relevant activities, they are only part of the psychological exploration needed in a cancer pain clinic. A less obvious, but equally essential, function of the psychologist is to help the team to better understand the meaning of pain for the patient.

Cancer Pain: A Symptom or a State of Being?

It is commonplace to refer to pain management as symptom control and to give the impression that alleviating pain is primarily, or exclusively, a matter of relieving or reducing a noxious physical stimulus. When we view pain management as a disturbance in the patient's quality of life, alleviating pain is understood as a comprehensive endeavour that influences the patient's entire state of well-being or sense of self. When the team addresses the patient's needs using a multidisciplinary, multimodal approach, its aim is to support and enact total well-being. Thus, the challenge of working with the cancer patient in pain is not just to relieve a physical symptom, but to improve the quality of life.

---

*Psychologist, Sunnybrook Health Science Centre; and Consultant, OCTRF Toronto-Bayview Regional Cancer Centre.

Generally pain is thought of as a multidimensional phenomenon, which includes the patient's physical, emotional and psychological suffering. Although we often accept this multidimensionality as self-evident, we need to remember that this way of thinking about pain has important clinical implications. It highlights the fact that appropriate interventions must maintain an individual focus based on the whole story of the patient's suffering—not just the medical facts—and addressing, as far as possible, the patient's whole problem. Individuals have their own unique histories, personalities, social and cultural contexts, and experiential perspectives—thus our interventions always must take place within this personal matrix of meanings and responses.

What Does Pain Mean to the Patient?

The individual can interpret pain associated with cancer in many ways, and it is critical that the caregiver have some understanding of how the patient thinks about his or her pain, and of strategies to deal with it. The rest of this paper will discuss some of the common meanings of pain we have encountered and some of the interventions we have developed to meet patients' concerns and anxieties.

"Pain means I'm going to die—soon"

For some patients, regardless of the person's actual physical status, pain is a sign of or is associated with imminent death; it means "I'm getting sicker and I'm going to die". Sometimes, pain is a sign that death is near and such patients may need help in dealing with their despair, anger, or sense of hopelessness. Relieving the pain with analgesics may allow these feelings to emerge more fully into awareness, so that patients may feel more emotional distress than before the physical pain had been relieved. The pain clinic may be one of the few places where patients can express openly their fears and anxieties about dying. To be reassured that the members of the team understand their fears, and that they are taking steps to manage the pain and suffering will do much to restore the patient's sense of control over events. Thus it is important during the clinic visit to provide time and an opportunity to discuss these feelings and, at times, for team members to encourage the patient to express such feelings.

To a subset of dying patients, pain relief means they are getting better and, believing this, they may stop taking their pain medication. Then the return of pain can be a devastating confrontation with the reality of their illness, suggesting to them that there is no hope for a cure or remission. Their despair, which is particularly poignant, often alternates with a determined denial of their terminal state. The caregiver needs to take special care to emphasize the need for continuing pain medication, without destroying the patient's fragile defences. He or she may suggest that the patient take analgesics again, without undertaking a detailed discussion of the underlying disease state. Nevertheless, this is a delicate task that often does not have a totally satisfactory outcome.

Some patients associate pain with imminent death, even when there little or no medical evidence that this is the case. They may believe, mistakenly, that doctors prescribe drugs like morphine, etc., only for dying people. A review of the patient's medical status may not relieve his or her anxieties completely, although it may help when combined with pain control and education about narcotics. If these measures fail, it usually is helpful to explore more fully the expressed fear of dying and to determine whether the patient's anxieties reflect other fears, which previously nave been concealed. With some patients, the concerns so uncovered may require referral for more extensive work with the psychologist.

"Pain means no one wants to, or can, help"

Sometimes, patients believe that their pain indicates that medical caregivers have failed to provide adequate care, have done something wrong, or simply don't want to help. They may be convinced that no one cares enough to address their needs or that there is nothing anyone can do after so many unsuccessful efforts. These patients may be angry, defeated, and resistant to the idea that over time the staff can achieve better pain control. As such, they can be particularly abrasive and aggravating to the treatment team. With these patients, the first step is to establish a working alliance through sympathetic listening—often these patients "come around" when they see that so many professionals are willing to listen and to understand. However, if pain control is incomplete, they may again resort to blaming the caregivers, and the caregivers may relieve their frustration by blaming the patient. Here the psychologist acts as a neutral intermediary, because often the patient sees that he or she is not responsible for medical decisions. Emphasizing that everyone on the team is frustrated and unhappy about the failure in controlling the patient's pain helps to diffuse blame and re-establish the alliance. In some patients, pain is never controlled satisfactorily; for them, a few extra minutes with the psychologist provides an opportunity for emotional ventilation and a chance to discuss coping strategies before they meet with the rest of the team.

"Pain Means There's No Control"

The sense of personal control, and how it is achieved and maintained, are central issues in all work with the cancer patient. Each patient defines "being in control" individually and subjectively, thus people differ in both the kind and degree of control which permits them to feel comfortable. For example, some patients prefer to leave all decisions about pain management to their caregivers—they will follow their medication regimen rigidly and will not adjust their schedule, even to cover "breakthroughs". One may need to monitor these patients closely to keep their medication levels at an optimum level (because the patient will not automatically titrate, even when given explicit instructions to do so.) and to assess for other factors associated with loss of pain control. Such patients also may tend to under-report the pain they do experience in order to appear compliant. Because they do not want to "criticize" the medical staff, they may be more willing to discuss deficiencies in pain control with the psychologist, who can then alert the rest of the team. On the other hand, patients who let the team make all the decisions sometimes blame them for failures in pain control and stop trying to find ways to relieve their own pain.

Although the desire for control is expressed along a continuum, some patients seem to have an intense need to exercise control of all aspects of their management. For them, pain that is "out of control" is a very disturbing experience, but they may be reluctant to consider interventions in which they can exercise little personal control, for example, the use of narcotic analgesics. If they anticipate side-effects like drowsiness or lack of mental clarity, the sense of diminished control is exacerbated. Often these patients collaborate actively in pain management—they will titrate their doses and closely monitor the balance between pain control and noxious side-effects; however they do need to feel that the pain team respects a patient's right to make his/her own decisions (within ethical limits), even if the team does not agree with them. The situation becomes more complex when other family members want more control or when a patient, who in the past has taken control, suddenly wants to shift responsibility on to a family member. The psychologist can help to negotiate a mutually acceptable agreement or to smooth the transition of control from the patient to other family members.

Conclusion

The challenge of developing an effective plan for the control of cancer pain should be based on a good understanding of what that pain means to the individual patient. This paper has described a few of the dominant themes we have encountered with our patients. Because each patient comes with his or her own unique personal thoughts and feelings, there is no "typical" pain patient. Only through careful and sensitive listening, can the caregiver hope to understand the concerns of the individual patient. We must keep in mind that those concerns may change over time or with progression of the disease. The team approach is well suited to this endeavour; individual team members bring not only their specific skills, but also their individual commitment to a co-operative and comprehensive solution to the patient's suffering.

PATIENT CARE DELIVERY SYSTEMS: "SUPPORTIVE CARE" IN PRACTICE

L.J. THOMPSON, M.Sc.N.*, *Toronto, Ontario*

In health care today we are challenged to provide the highest quality of care within a fixed envelope of funding, which seems to get smaller as patients needs get larger and more complex. In this environment we struggle to pay comprehensive and well co-ordinated attention to quality of life issues in everyday clinical practice. In trying to do more with less, we need to look hard at what we do for patients, but also need to assess the impact of our interventions on patient outcomes. These outcomes relate not only to survival—number of years added to a patient's life, but also to the quality of the **life** added to those years.

Ginsberg[1] defined supportive care as that in which "the quality of life of those patients referred to our care is preserved, or even enhanced, and whereby their adjustment to the altered reality that the diagnosis produces is facilitated". Support of patients and families with complex and multidimensional needs requires comprehensive and continuous care by a team of caregivers who possess a range of knowledge and skills. No one health care provider can do it all. We need a mode of organization, which maximizes the potential of each team member, so that two or more contributors can achieve more than any one could do on his/her own. If we co-operate more effectively, we can do more with less, while at the same time improving our outcomes part of which is attention to the patient's emotional and psychosocial needs.

This paper will provide a brief overview of issues and challenges associated with various patient-care delivery systems, which seek to translate the philosophies of psychosocial oncology and palliative care into day-to-day service. It will review some of the existing models and look at models of the future seeking insight into opportunities for growth within the Ontario Cancer Treatment and Research Foundation (OCTRF) system.

The term "patient care delivery system" describes the framework in which professional services are organized. Those who design such systems need to consider the complex and multidimensional needs of people with cancer. The ambulatory care environment offers a variety of challenges because the interaction with patient is episodic. In this type of setting, the caregiver does not have much time to get to know each patient as he/she does in hospital. When the patient visits the cancer centre, we need to maximize those brief encounters so as to identify the physical, psychological, sexual, spiritual and social needs and make plans to assist patients and their families to meet those needs.

---

*Director of Nursing, Toronto-Bayview Regional Cancer Centre; and Assistant Professor of Nursing, University of Toronto.

The OCTRF regional cancer centres are committed to the philosophy and principles of primary nursing (PN)—a system of care which makes nurses accountable for individualized outcomes in a defined caseload of patients. PN includes independent nursing management of patient care issues, triaging of problems and referrals to other support staff and the overall co-ordination of patient activities as they relate to the individual's treatment plan. Primary nurses focus on specific patient populations, which are clustered by disease site, by physician or sometimes a combination of the two. At some centres, when individual patients receive treatment or require inpatient care, their care is then co-ordinated by nurse consultants in these specific areas. During this time, the primary nurses maintain contact with the nurse consultants and collaborate especially in the planning of care for patients with complex problems. At the Toronto-Bayview Regional Cancer Centre, nursing is moving toward a group practice model, whereby all of the nurses who "share" a patient get together for conference, which focus on clinical problem-solving and evaluation of patient outcomes.

In the OCTRF patient care delivery models, PN is a consistent link and support system for patients and their families throughout their experience in the cancer system, which may extend from diagnosis until after the patient's death. The primary nurse is in constant communication with the patient's oncologists during and in between clinic visits, so that between them they can deal with acute problems quickly and effectively. The nurse-physician relationship varies from team to team, depending on personalities, patient needs, degree of mutual trust and respect, and the degree of collegiality. Not all teams enjoy a true collaboration, however most team members try to complement the functions of the others, so that their teamwork will enhance the overall care of patients. Patients are introduced to the team early in their stay at the cancer centre, so as to make clear the role of the nurse in relation to the physician.

With respect to the disciplines of social work, psychology, clinical nutrition, radiation therapy technologists and pharmacy, there is great variation among the various centres in the degree to which these groups are integrated into the overall patient-care delivery system. In 1989, the OCTRF report on supportive care of patients with malignant disease in the Ontario regional cancer centres[1] identified resources available in each of the cancer centres, evaluated the effectiveness of existing programs and made specific recommendation for all centres. This report provided an excellent framework for the development of supportive care initiatives in the centres, yet there are still many deficiencies, in particular, there is little integration of supportive care services into the "big picture" of cancer care. Typically, nurses are responsible for identifying and assessing clinical and other needs and co-ordinating referrals to social work, nutrition etc., however because there is considerable ambiguity about roles and authority, the type of referrals are not always consistent and the patient's care may be fragmented or focused on crises. If we learned better how to identify high-risk patients, and to integrate assessments of the risks of various forms of supportive care into the "standards" care of cancer patients, then we could integrate the interventions of different caregivers so as to enhance patient outcomes.

Considering the financial and other stresses that erode the current systems of care, what should we be working toward for the future? In all of our patient-care activities, we are being scrutinized by a variety of regulatory bodies especially with respect to patient outcome; hence we are challenged to demonstrate the effectiveness of care, with respect to both patient's needs, and the organization's needs.

To meet some of these challenges, some centres in the United States and Canada have adopted a "new" model known as case management. This patient care delivery system focuses on achieving certain outcomes within stated time frames and with economical use of resources. Case managers are held accountable for the entire episode of illness and they have authority in all settings where the patient receives care[2]. This model has been referred to as "second-generation primary nursing", one of the principal differences between this model and traditional nursing is the extension of accountability beyond a given shift or clinical unit. In this model, the physicians still direct overall medical care, however they work collaboratively with case managers to determine clinical indicators of patient outcomes, and set appropriate timelines for their achievement. Case managers collaborate with other nurses and allied health-care professionals to plan for the achievement and evaluation of psychosocially related patient outcomes. In most models, the nurse functions as the case manager because her/his clinical skills of patient assessment, analysis and interpretation of interventions, co-ordination and teaching all lead to the kind of accountability desired of case managers.

This brief overview of primary nursing and case management can but illustrate some of the issues we face within OCTRF as we evaluate current systems of care. No one system is a panacea. Certain elements of primary nursing and others of case management need to be examined as the character of ambulatory cancer care shifts. Those concerned about supportive care for people with cancer, and the contribution of the professional staff within the cancer centre to that care, need to take a system-wide view of patient care delivery models. No longer can we afford the "parallel play" of oncology nurses, physicians, psychologists, social workers and others. We need to make better use of our specialized resources so that each realizes his/her full potential. Patients need access to different caregivers with distinct ranges of knowledge and skill, however the work of these caregivers must be integrated into a model that is acceptable to both patients and caregivers. As our centres get larger and patient care gets more complex, accountability for care may become diffused and consequently it becomes more difficult to evaluate the outcomes of care. As professionals, we are accountable for the full range of needs our cancer patients and their families have, and we must use creativity and wisdom in deciding how we will meet those needs. There is always a new or revised delivery system on the horizon, and we must take the time needed to analyze and evaluate their respective risks and benefits before we alter our current systems. In these difficult times, we need to balance patient advocacy roles with resource utilization and management functions. In the OCTRF-OCI/PMH systems, we are positioned to provided leadership for cancer care that encompasses the medical and supportive care dimensions of practice and research. Through our collective efforts, we can bring alive the vision of comprehensive cancer care in day to day practice.

REFERENCES

1. Ginsberg AD: Supportive care of patients with malignant disease in the Ontario regional cancer centres. 1989. (Internal document of the Ontario Cancer Treatment and Research Foundation)
2. Zander K: Collaborative care: Nursing case management. 1989. (American Hospital Publishing Inc. USA)

ENHANCING THE QUALITY OF LIFE OF THE CANCER PATIENT AND THE ONCOLOGIST: REFERRALS TO THE PSYCHOLOGIST—WHO AND WHEN?

R.A.A. BUCKMAN, M.B.,Ch.B.* and B.D. DOAN, Ph.D.**
Toronto, Ontario

They're Needful, We're Busy

In the care of the cancer patient, there are very few statements that can be made with absolute certainty. Two of them: (a) oncologists seem to be working harder and harder, and (b) patients' needs seem to be increasing. In this article we shall put foward a small number of practical suggestions for reducing the pressure on the oncologist and perhaps meeting the needs of the patient with greater flexibility.

The psychosocial needs of the cancer patient are both multiple and multifaceted. Interdisciplinary teams in oncology are also many-faceted and often are multitalented. Nevertheless, typically the front-line responsibilities of care fall on the oncologist and nursing staff, so that physicians and nurses function under a good deal of strain. On the one hand, they have to attend with maximum efficiency to the complex and often unpredictable physical needs of their patients. On the other hand, they are obliged to treat each individual patient ***as a person***, and to provide that individual with compassionate care, understanding and reassurance. They do all this in most instances with considerable empathy for the plight of the person with cancer and his or her family. Cancer care can be heartbreaking work.

On many occasions, the oncologist and nurse are faced with patients whose suffering and needs for assistance exceed the capacity of the busy clinic. When the medical team is aware of the patient's difficulties, but cannot accommodate them, this may lead to a feeling of helplessness. In addition, some patients present problems which are beyond the training and capability of the nurse or physician. If any of us are spending our time doing things that we are ***not*** good at, clearly we are not using that time to do the things we ***are*** good at. When our own feelings of frustrations and helplessness increase, so, perhaps, does the patient's distress.

---

* Medical Oncologist Toronto-Bayview Regional Cancer Centre.

** Co-ordinator, Psychology Services to Oncology, Sunnybrook Health Science Centre.

Difficult Patients or Difficult Situations?

As the illness progresses, and the patient's health deteriorates, and the possibility of dying becomes more real, things become more difficult. Emotional temperatures rise and patients frequently direct their anger or frustration at the health-care professionals (*"blaming the messenger for the bad news"*). In these circumstances, caregivers are challenged to distinguish the extent to which they are dealing with a difficult patient or a difficult situation. The risk of *"blaming the victim"* rises accordingly. The health-care team tends to react defensively (for example with hostility) or by partially withdrawing from the patient. Invariably this increases the patient's sense of isolation and of unfulfilled needs, and increases the professional's sense of frustration and harassment.

Clearly, one way of reducing the oncologist's burden is to share the load by involving other disciplines such as psychology. However, the frequent reluctance to make such a referral may have several sources:

(1) It is difficult to be sure which referrals will be successful and produce a benefit. Most health-care professionals are reluctant to refer if it is not going to benefit the patient, because it not only wastes the patient's and the referring physician's time, but also diminishes the patient's faith in the team;

(2) The physician may not be sure if this patient's problems fall within the psychologists' domain, or even which referrals psychologists most actively seek; and

(3) The physician may be concerned that the act of referral would reveal or emphasize any deficiencies (real or perceived) in his or her management.

For all these reasons, there is often uncertainty about which referrals are most appropriate, which patients are most likely to benefit and at which point in the disease a referral is most likely to help. Nonetheless, a timely referral can produce major benefits. In itself, a referral to help address the patient's expressed difficulties acknowledges and validates the patient's personal concerns. That acknowledgment alone can strengthen the patient's faith in and relationships with the referring physician and nursing staff. The additional time spent with the psychologist invariably contributes to relieving the patient's distress, and—as has been demonstrated in other outpatient medical settings—contact with the psychologist can reduce overutilization of medical services in the cancer centre. In addition, many patients feel grateful to the medical and nursing staff, who are helping them to survive, and hence are reluctant—and at times unable—to share their deepest concerns with them for fear of "letting the team down". Usually such patients welcome the opportunity to meet with the psychologist to grapple with issues and express fears that he/she is unlikely to share with the health-care team without loss of dignity and feelings of self-worth.

In what follows, we shall outline those clinical situations in which referral to a psychologist, may fe of value basing our suggestions on some of the current practices at the Toronto-Bayview Regional Cancer Centre.

What Does the Psychologist Do, Anyway?

The consulting psychologist† in a cancer treatment centre is ***not*** there to supplant or hinder the oncologist and nurse from providing whatever psychosocial care and support they are able. The psychologist brings additional expertise to the assessment and treatment of the psychosocial problems that come with cancer. Thus the psychologist ***complements and extends*** the team's ability to meet more adequately the major psychosocial needs of persons with cancer and their loved ones.

Clinically, the psychologist assists patients and families to cope with acute and chronic health crises, to facilitate their adaptive efforts and promote their psychological well-being. They are consulted about a variety of difficulties—from specific reactions to treatments and their effects, to more profound existential concerns related to self, important others, and the prospects of an uncertain future. Whatever the presenting problem, the psychologist will approach it in light of the concrete realities of the illness, taking into account who the patient is and the nature of his/her social reality. He or she helps the patient to deal actively and constructively with issues and difficulties arising from the illness, helps to minimize emotional distress, and helps the person with cancer to maintain the best balance between personal autonomy and reliance on caregivers and loved ones.

Usually the psychologist carries out these functions as a member of the multidisciplinary team. At the Toronto-Bayview Centre, for example, three psychologists have been assigned to the pre-existing disease-site teams. They have developed close working relationships with the oncologists, nurses, social workers, pharmacists and other health-care staff involved with a given disease-site. They attend the case-conferences, and provide patient-consultation on a referral basis for a given disease-site, and in the case of the Centre's cancer pain consultation service, routinely attend the weekly clinics. In some other cancer centres, psychologists and social workers operate within a centralized psychosocial resource team, providing clinical service to various disease sites on a referral basis. In both cases, the psychologists' effectiveness depends substantially on the degree to which they function as integral members of the broader team.

---

†To become a psychologist, he or she will have earned a doctoral degree in psychology. With an average of nine years of intensive academic training in an approved postgraduate program, the psychologist will be knowledgeable in the biological, mental, emotional and social bases of human behaviour, proficient in research design, methodology, and statistical analyses, and will have skills applicable to areas of specialization. The psychologist will have completed an additional year of supervised training beyond the doctoral degree, and been evaluated much as is an interning physician or articling lawyer. He or she will then have passed written and oral examinations administered by a government-appointed Board of Examiners in Psychology. The psychologist's professional conduct is regulated by strict ethical rules and practice standards specified in the *Psychologists' Registration Act*.

Clinical Situations in Which Referral is Most Useful

1. The Patient Who is Not Coping.

Almost every clinician will recognize the patient who "is not coping" although it is a difficult condition to define. Its most salient feature is that the patient's emotional state inhibits his/her ability to make decisions and to draw up rational plans. The most common underlying emotional states are anxiety and depression, but frequently the patient presents blends of grief, anger, guilt and other strong emotions. The patient's distress may be obvious and he/she may show the physical signs of anxiety—tachycardia, tachypnoea, hyperactivity, and so on. Usually the patient has an adequate or even excellent grasp of the medical facts, but feels overwhelmed and may be unable to plan or carry out a rational course of action. Thus the cardinal signs are a failure of decision-making capacity and a strong emotional response to all or most obstacles or reverses.

Objective of referral: To help the patient to identify the major unsolved problems, to evaluate her or his coping strengths and deficits and to use relevant coping strategies more effectively. In responding to such referrals, the psychologist usually will focus on helping the patient to better regulate her or his emotional distress, and then assist her or him in active problem-solving.

Probability of Positive Outcome: Moderate to high, especially with timely, that is, early consultation.

2. The Patient Who Appears to be "Unfixable".

Sometimes called *"the heartsink patients"*, they seem locked into a maladaptive pattern of reacting to circumstances; this pattern seems to be ingrained even though it only adds to their distress. Often the patient has little insight into the ways in which personal responses contribute to the coping difficulties, seems to have little motivation to change, and seems to have little flexibility for negotiating change. In these circumstances, it is unlikely that the oncologist can reduce the patient's distress, and often he/she may feel guilty and inadequate for "letting the patient down". When an oncologist senses that a patient's psychosocial problems are significant and "unfixable", it can be most useful to refer the patient to a psychologist for a second opinion. If this confirms the oncologist's clinical impressions, the psychologist may be able to suggest constructive ways of managing the patient. The patient may not improve, but the patient-practitioner relationship will.

Objective of referral: To confirm that no further measures are likely to relieve the patient's distress.

Probability of a positive outcome: High. In our own setting, one oncologist has estimated that about two-thirds of his referrals are for second opinions about "unfixable" problems. Quite independently, the psychologist estimated that no intervention was possible in only 10% to 15% of the cases. In most instances, at least some portion of the patient's difficulties are amenable to change, and thereafter we notice at least some improvement in the patient's interactions with clinic staff.

3. The Patient with Unfinished Business.

Most oncologists are familiar with the patient who comes encumbered with unresolved, premorbid emotional difficulties. They may stem from parental conflicts, particularly in patients in their 30s and 40s, pre-existing marital dysfunction, conflicts with other family members, or social circumstances characterized by significant role strain, e.g., a single, working mother, who also bears sole burden of caring for aged parents. The cardinal signs are not always easy to detect. At first, patient's distress may be difficult to explain or account for, usually because it is not consonant with the patient's medical situation. For example, the patient may be unexpectedly withdrawn, or continuously angry, in spite of effective treatment or a favourable prognosis. In such circumstances the patient's distress may affect adversely self-care or adherence to cancer treatment. Referral may be most useful when there is a hint of major, unresolved business; sometimes the first indication comes from another health-care professional, or sometimes from a family member.

Objective of referral: The resolution of the unfinished business.

Probability of a positive outcome: High to very high. In most cases, brief, problem-focused psychological intervention will be sufficient to help patients to address maladaptive familial and interpersonal difficulties. A further benefit to the health care team results from the partitioning of the patient's sources of concern: concurrent contact with the psychologist to take care of unfinished business will almost always reduce the intrusiveness of those problems during clinic visits.

4. The Patient Who Needs Somewhere to Cry.

Some patients carry a heavy load but can cope with it if they have a place where and a person to whom they can express their fears and receive help in resolving important issues, which have arisen as a consequence of their illness. Frequently, such a patient is the "coper" of the family and until then has been perceived as its strongest member. When forced by cancer to accept care, he/she may believe that no one else in the family is able or prepared to assume the caretaking role, or to accept alterations in the patient's role as primary caretaker. For instance, the patient may have a spouse who cannot cope with tears, sadness, pain or fear, or is unprepared to take on additional responsibilities in the home. "Copers" may have a strong emotional investment in their role in the family and hence may resist the care and support of loved ones. The patient may feel guilty about being "weak". In this situation referral gives the patient "an hour a week to unload, and a professional shoulder to cry on". Typically such patients are uncomfortable about expressing their fears or feelings of despair with clinic staff. They may fear that they are "disappointing" their oncologist by appearing less than strong and, if this happens, may feel diminished as persons. Frequently, clinic staff discover their private distress accidentally, when temporarily the patient loses his/her composure. While one should not over-react to a patient's tears, the offer to refer them to a psychologist provides him/her with needed emotional support, and also allows the patient to maintain self-esteem and a sense of dignity.

Objective of referral: Ventilation and emotional support.

Probability of a positive outcome: High to very high. In most instances, regular contact with a psychologist restores a sense of control and allows the patient to resume previous roles and functions, if only in part. Where appropriate, the psychologist will intervene to help the patient and family adjust their new relationships with one another, and prepare better for the future.

5. Heroic Self-healers.

At present, the concept of self-healing is popular and many patients and family members now believe that a cancer patient's state of mind has a direct effect on the course of his/her disease. In particular, patients are inclined to believe that positive thoughts and feelings and a fighting spirit are necessary for self-healing. When patients attempt to heal themselves during a period of medical stability, they usually cope well. However, if a patient begins to deteriorate, he or she may perceive the progression of the disease as evidence of his or her own failure. The guilt and self-recrimination (or even blame by others), which may follow, may be severe.

Even during disease-free intervals or while off treatment, some patients' efforts to heal themselves creates distinct problems. For example, a proportion of patients will interpret far too literally the popular exhortation to think positively, (i.e., at all times,) and become fearful that thoughts about cancer or death might cause the disease to progress. Distress over this negative thinking then may produce further alarm in the patient struggling to maintain a heroic stance, leading to impaired coping and persistent, escalating anxiety. In these instances, timely intervention by the psychologist can be extremely effective.

Objective of the referral: To provide the patient with expert advice concerning the benefits and hazards of adjunctive psychological strategies, to restore the patient's coping and to assist him/her in coming to terms with the realities of this illness.

Probability of a positive outcome: High. Our psychologists have adopted a person-centred approach to self-healing techniques. When these strategies are enhancing the patient's sense of control and emotional well-being, they support and reinforce these efforts. If these techniques are producing increased anxiety, guilt, or alienation, the psychologist will intervene with more effective ways for the patient and significant others to participate in his or her care, and prepare for the future.

Clinical Situations in Which Referral is Unlikely to be Fruitful.

Patients with pre-existing major psychiatric illnesses should not be referred to a psychologist but should be seen and assessed by a psychiatrist. If the current psychiatric illness is stable or insignificant, then a psychology referral may be effective, but the psychiatric consultation should be obtained first. Similarly, it is unlikely that the demented patient will benefit from psychological consultation, although family members may welcome the opportunity to consult.

Also, referral to a psychologist is unlikely to be of much benefit in the patient near the end of life. Often elderly or preterminal patients are preoccupied (appropriately) with their physical state and may not have the energy or mental resources to establish a therapeutic relationship.

When to Refer

Although highly distressing, most people deal from their own resources with the discovery of a tumor, having it diagnosed as malignant, and receiving primary treatment, or have the support of family, friends, and front-line health care staff. If they seek consultation with a psychologist during this period, usually it is for specific problems—for help in coping with treatment toxicity, for information on adjuvant psychological treatment, for help in adjusting to the loss of a body part or function, or because of pre-existing personal and social conditions which have increased emotional or adaptive difficulty.

For the most part, during the initial phase of cancer illness distress tends to be acute and of limited duration. Perhaps at this time the patient's distress is mitigated by the attention received during admission and primary treatment and, more often than not, is offset by the optimistic, curative stance adopted by the caregivers. There are exceptions, of course: Some patients know that their prospects are bleak from the outset. However, most seem to manage relatively well without referral to a psychologist during the primary treatment phase of the illness.

The best time for referral is when the patient's distress is interfering with his/her life. Typically, in our Centre we make referrals to the psychologist. 1) After the initial shock of diagnosis has passed and the patient is nearing the end of treatment; 2) in the disease-free interval when the patient has no symptoms but is living under the threat of recurrence; or 3) at the time of first relapse. This seems to us to make a good deal of sense when one considers the uncertain, ambiguous nature of their situation, the pressure to resume normal life despite residual treatment toxicity and morbidity, diminished attention from caregivers and friends, and unresolved issues provoked by the discovery and treatment of their cancer. During this period, the oncologist is most likely to become aware of the patient's distress, and patients are most likely to welcome and make optimum use a psychological consultation.

Concluding Remarks

Because of their training, oncologists seem to believe that they ought to be able to provide almost everything for almost everybody. Often they are made to feel inadequate (by their patients or society at large) when they cannot. Appropriate use of the psychologist and other experts can lighten the load and provide some relief and support for the oncologist as he/she struggles with a difficult job. We will always be busy, the patients will always be needful, and we will continue to do what we can to support and reassure them in their plight. Effective use of the consulting psychologist is one way of extending and providing more comprehensive, flexible care to persons with cancer and their loved ones. With appropriate referral, we can all be better served and less stressed.

STRESS AND COPING IN CANCER PROFESSIONALS

MARY L.S. VACHON, R.N., Ph.D.*, *Toronto, Ontario*

Health-care professionals working with people with cancer are often are asked: "Isn't it very depressing to do this work?" or "How do you cope when you are exposed to so much death and suffering?" This paper will review some of the sources of stress for health-care professionals in the field of oncology, the ways in which their stress is manifest and the coping mechanisms they find useful as they continue in this work. The data use in this paper are part of a larger set, which I gathered during an international study of 581 caregivers[1].

A model helpful in understanding occupational stress in cancer is that of person-environment fit derived from the work of French, Rodgers and Cobb[2]. These workers assert that adaptation is a function of the "goodness of fit" between the individual's characteristics and those of the work environment. They assess "fit" in terms of the concordance between the needs of the individual and the resources available within the work environment, between the abilities of the individual and the demands made by the work environment, or between both pairs of these variables.

In assessing one's own goodness of fit within a specific environment, the individual must be able to assess both self and work environment. Individuals need an accurate understanding of their own resources, values, and limitations and of the resources available in the environment to meet their needs and to help them perform as professionals[3].

THE STUDY

The 110 professionals, who were working in cancer care and were interviewed, constituted 39% of the total international sample of 581 caregivers. Table I shows the group's professional background, age and work setting.

These subjects were interviewed individually or in small groups. They were told that the interviewer was writing a book on the care of the critically ill, dying and bereaved; they were asked to comment on the stressors encountered in the work situation; how personal variables such as age, religion, social support, personality and previous or concurrent stressors affected their response; how their stress was manifest and how they coped with stress.

TABLE I

CHARACTERISTICS OF CANCER-CARE PROFESSIONALS

	NUMBER	PER CENT
Profession:		
Medicine	38	35%
Nursing	33	30%
Counselling	18	16%
Other	21	19%
Total	110	100%
Age (yrs):		
<30	11	10%
31-45	63	57%
>45	36	32%
Practice Setting:		
Teaching hospital	87	79%
Community hospital	11	10%
Community agency	12	11%

Personal Mediating Variables

Age. For all the age groups, the major stressors were those related to the work environment. The younger caregivers reported more stressors, more manifestations of stress and fewer coping mechanisms. Older caregivers reported fewer stressors, fewer manifestations of stress and more coping mechanisms.

Social Support. Regarding the value of social relationships in mediating work-related stress, the respondents were more likely to identify a lack of social support or problems in their personal support system (60%) than to mention that home relationships were helpful (40%). One oncology nurse noted "I feel that I can't verbalize some of the problems I face at work to my family, as well as patients and co-workers".

Previous Stressful Life Events. Previous life experiences can influence one's career choice, for example, when a parent has died of cancer the child may decide to enter the field of oncology. Caregivers often reported that personal experiences with illness and/or bereavement had given them an increased understanding of patients. However, if such experiences were unresolved, they might overidentify with patients and families.

Concurrent Stressors. Current stress may give caregivers either more or less energy to cope with work-related problems. Sometimes caregivers believed they got relief from family problems by coming to work. At other times, however, problems at home made it difficult to concentrate on one's work. The major concurrent stressors reported in this study were: Illness or bereavement in family or in a friend; conflict within one's marriage or in a close relationship; personal problems, such as health concerns, divorce or separation, and family problems.

Stressors Within the Work Place. Caregivers in oncology were different from those in most other settings in that the stressors they reported did not come from any specific aspect of their work such as the environment, occupational role, patient/family or the disease. Rather, their stressors were divided evenly among three major areas: Work (30%); occupational role (30%); and patient/family (30%). Disease-specific stressors accounted for 10% of these (Table II).

Patients and Families with Difficulties in Coping or with Interpersonal Disorders. These patients and families give caregivers increased difficulty. They mentioned such problems as patient/family depression that, although understandable, sometimes was difficult to bear; anger that might reflect the fear, which patients and family felt; withdrawal that often appeared around recurrence or the approach of imminent death; and psychotic behaviour, which often reflected an underlying disease- or treatment-related conflict. Particularly, stressful for caregivers were those who denied their disease; those who acted-out with such behaviour as drug or substance abuse or not "responsibly" following treatment regimens; those who avoided dealing with their disease; and multiproblem families.

TABLE II

STRESSORS IN ONCOLOGY

- Patient/family difficulties in coping or interpersonal disorders
- Patient/family difficulties in communication
- Role overload
- Team communication
- Identification with patient/family
- Role ambiguity
- Role conflict
- Inadequate resources
- Communication problems-others
- Unrealistic expectations of organization
- Lack of control

Patients and Families with Difficulties in Communication. Under this category were patients with brain tumors, who no longer were able to communicate with caregivers, those of a different religious background and/or those with an unusual value system. Caregivers also had difficulty if the patient/family were similar to the caregiver. Strong identification may make it difficult to reach clear decisions about treatment and/or to decide on management when the patient enters upon the weeks before death.

Role Overload. A common experience by workers in oncology is role overload—the feeling that one has too much to do. Often this syndrome is encountered in those who attempt to combine clinical work, research, publishing and teaching. Sometimes these caregivers recognize and can acknowledge that this state is self-induced. As one oncologist said, "We start dancing to a tune that you're called to play by yourself". Often it is difficult to remove or reduce this stressor if workers in oncology caregivers have taken on multiple roles as a coping strategy.

Team Communication. Difficulty in communicating with other team members is reported less often among oncology staff than in other specialties. These conflicts relate to difficulties in developing trust among members of the team; difficulty in communicating information; power struggles; difficulty with conflict management and "incest" among team members.

"Incest" might consist of sexual relationships but also may involve the imposition of communication patterns developed in one's family onto other team members.

Other Work-Related Stressors. The survey brought to light the following: Identification with the patient/family or the awareness that this patient could be me or a family member; role ambiguity *viz* failing to identify one's true role; role conflict, the struggle to balance conflicting roles within one's profession, between one's personal and professional life, or between one's professional life and one's personal value system; the frustration of working with inadequate resources and/or staffing; difficulties in communicating with other specialties or with other departments; the organization's unrealistic expectations and a lack of control over one's work environment.

DISCUSSION

This stress was manifested as feelings of depression, grief and guilt, which the professional felt not only in response to a patient's death, but also it was reflected in a loss of self esteem—a sense that I had not performed up to my self-imposed standard. In addition, the worker sometimes experienced depression, grief and guilt when his/her colleagues failed to support or recognize them.

Anger irritability and frustration were common among workers in oncology. Often these caregivers realized that much of their anger came because they were feeling frustrated and didn't know what to do with their feelings.

Often work-related stress was manifested in job/home interaction, that is taking one's work stressors home at the end of the day. These caregivers described feelings of helplessness, insecurity or inadequacy and at times acknowledged that they dealt with stress by avoiding either their patients or their families.

The most common of these coping mechanisms, as in most other health-care specialties, was a sense of competence, control or pleasure in one's work. This sense was associated with the feeling that the individual had been able to do "as well as can be expected given the circumstances". Often those caregivers felt they had some control over their environment and could derive pleasure from their work.

Developing multiple roles, which is an important coping mechanism in oncology, also may act as a stressor.

A personal philosophy of illness and death is essential if a professional is to survive in oncology. Some have adopted the philosophy expressed by Weisman "Don't worry, your time will come. What can you do today when it isn't your turn that you hope that someone else will do for you when it may be"[4].

A sense of team philosophy, support and team building also were important in survival. Teams, whose members had worked out effective role definitions and thereby had resolved conflict and had much less work stress.

Finally, when coping strategies, including lifestyle management failed, caregivers left their jobs sometimes for a short break, at other times permanently.

In conclusion, although work in oncology involves many stressors, many caregivers have concluded that the rewards of such service far outweigh the stress involved.

REFERENCES

1. Vachon MLS: Occupational Stress in the Care of the Critically Ill, Dying and Bereaved. Washington, D.C.: Hemisphere Publishing, 1987.
2. French JRP, Rodgers W, Cobb S: Adjustment as person-environment fit. *In*: Coelho CV, Hamburg DA, Adams JE, eds. Coping and Adaptation. New York: Basic Books, 1974: 316.
3. Vachon MLS, Stylianos SK: Caring for the caregiver: A person-centered framework. *In*: Baird S, McCorkle R, Grant M, Saunders WB, eds. Cancer Nursing: A Comprehensive Textbook. Philadelphia: W.B. Saunders Company, 1991: 1084.
4. Harrison RV: Person-environment fit and job stress. *In*: Cooper CL, Payne R, eds. Stress at Work. Chichester: Wiley, 1979: 175.

THE PLACE OF SOCIAL WORK IN PSYCHOSOCIAL ONCOLOGY

A. SAWARNA, M.S.W.*, *London, Ontario*

From its initial diagnosis to death and bereavement, cancer affects not only patients, but their spouses, children, relatives, friends, employer and co-workers. Faced with sudden uncertainty, patients and those close to them often feel a loss of control, anxiety and stress.

Working closely with physicians, nurses, and radiation technologists, the social worker helps patients and their families cope with altered circumstances, anticipate and deal constructively with problems arising, recognize and use their resources and strengths, and find additional resources where applicable (see Appendix I). Fully appreciating the special problems associated with particular disease sites and "high-risk" patients, the social worker provides techniques such as adjustment therapy; resource, crisis and bereavement counselling; general support and psychotherapy; and relaxation and mental imagery. The social worker also treats problems unique to particular family members. For example, when a parent is seriously ill or dying, children have a limited capacity for resolving fears and grief through therapeutic interviews. Thus the Centre provides play therapy for children aged 2 through 10, in a playroom furnished with toys specifically chosen to help them express feelings.

Social work is an integral part of the London Regional Cancer Centre's (LRCC) larger commitment to comprehensive patient care. On arrival, each patient is assigned to a site-specific multidisciplinary team. This assures the patient access to the same nurse, physician, dietician and social worker throughout his/her relationship with the Centre. Each discipline on the team brings its special expertise to the cases at hand. At the same time, the disciplines must be strongly interdependent for the correct functioning of the team. For example, social worker rely on physicians and nurses for much of the psychosocial screening of patients for "high-risk" cases, as well as for referrals. To effectively counsel patients and their families, social workers also must learn from physicians the problems associated with particular disease sites, and the physician's detailed prognosis for individual patients.

Thus social workers minister to the patient's psychological, social, and practical needs from a systems perspective. They serve primarily the individual and family but, where the need arises and staff resources permit, may serve groups; for example, one of these is for bereaved spouses and another, which operates through the Centre's Palliative Care Program, is for bereaved children. A third patient's education/support group was organized at the Centre's residential lodge five years ago. Meeting weekly, lodge residents hear presentations from the various cancer-care disciplines, including radiation technologists, radiation oncologists, nurses, dieticians, social workers, and the Lodge manager. In addition to helping patients to understand better their disease and treatment, the meetings enhance staff job satisfaction and minimize their personal and professional isolation.

---

*Manager, Department of Social Work, OCTRF London Regional Cancer Centre.

Beyond clinical work, social workers provide psychosocial cancer education for staff at the Centre and health-care professionals in the regional catchment area. To this end, they enhance understanding by the use of specially prepared video tapes. Also they stimulate discussion through vignettes about particular populations, such as bereaved children, breast patients, women patients, and palliative care families.

Preventive measures deserve more emphasis than current staff can provide. Despite our best efforts, some patients and families stumble into rather than anticipated emotional and practical issues pertaining to their particular type of cancer; this diminishes their prospects for feeling "in control". In these circumstances, we seek to expand social work services in two directions: i) a more comprehensive screening of patients at the time of entrance to identify "high-risk" patients and families; ii) in addition, to work with patient/family groups that have special needs, e.g., young adults with small children or elderly couples facing the loss of a partner. Our experience is that group work has considerable preventive as well as therapeutic benefit. As noted above, group work is rewarding for staff because it helps them to ward off "burn-out", an ever-present risk in this high-stress field.

Despite heavy clinical demands, the Department has undertaken a number of research projects: i) the systematic evaluation of the Department's services and interaction with the other cancer disciplines; ii) the targeting of service needs; iii) the routine generation of useful research data, so that these projects will be continuous rather than episodic; iv) the enhancement of the Department's information base for liaising with the other cancer disciplines, both at the LRCC and in other institutions; and v) the enrichment of the Department's relationship with programs in social work and oncology at the universities.

In support of these objectives, the Department is designing two interrelated projects: i) A detailed statistical comparison between the social work case load population and the larger total patient population at the LRCC; and ii) a quality assurance survey. Based on a model developed for the social work department at Wellesley Hospital in Toronto, the second project uses questionnaires to obtain evaluations of social work services from patients, the other disciplines at the LRCC, and referring agencies.

By establishing the first social work department at any cancer centre in Ontario in 1983, the LRCC led the transition from a physician-centred remedial approach to cancer to a broad multidisciplinary program of psychosocial oncology. The psychosocial program is preparing itself for further development. First, we expect an exponential growth in Ontario's cancer population. Second, the frequency of particular types of cancer will change in consequence of such demographic changes as population ageing, lifestyle and environmental changes, and breakthroughs in oncological research. At the LRCC, these services are administered predominantly through the Department of Social Work—a model that works well and will continue to be the focus for their development.

APPENDIX I

The Social Worker, Patient and Patient's Family Through Six Stages of Cancer Care: A Framework Used in the London Regional Cancer Centre

1. Discovery and Diagnosis

Patient-Family Task. Assess the significance of the diagnosis, e.g., the patient's expected length of life and/or permanent physical disabilities and how these impact on the material well-being of family members, job prospects and income, and personal relationships. Work through despair, shock, and strain, which may inhibit a constructive response.

The Social Work Focus. Help the patient acquire a realistic perception of his/her situation and feel "in control" when dealing with issues arising from it. This stage entails: i) helping the patient to manage important but potentially destructive emotions, such as frustration from dealing with the unknown, anxiety, sadness (acute depression), anger, and guilt; ii) helping patient and family to define role responsibilities, which minimize self-damaging behaviours and help them live with cancer; iii) arranging contact with appropriate community support systems; and iv) advising the family physician of our assessment and interventions.

2. Primary Treatment (Surgery, Radiation, Chemotherapy)

Patient-Family Task. Recognize and cope with realities presented by treatment. This entails adjustment to altered body shape and/or body function, which, in turn, has social and economic implications and may give rise to destructive emotions—feeling overwhelmed, shock, numb, denial, extremes of fight or flight. It also requires adjustment to the hospital milieu—the institutional atmosphere, jargon, procedures, professionalism, and learning how to reach out to others for support.

The Social Work Focus. Help the patient mourn the lost parts or functions, replace or compensate for them, and maximize other personal resources to maintain a sense of intactness and self-esteem; help patient and family to regulate their emotional reactions, interact effectively with each other, and adjust lifestyles to accommodate the patient's altered circumstances; serve as patient advocate in the hospital setting; help family members assert their needs in the system in order to negotiate it effectively; assess the family's social support network and initiate appropriate community referrals; and inform the family physician of information, which affects his/her relationship to the family.

3. Remission With Return to Normal Activity

Patient-Family Task. Strike a new balance in roles and expectations to facilitate a return to normalcy, while remaining aware of the risk of recurrence; cope with fear of recurrence.

The Social Work Focus. Help the patient and family to adjust their roles, expectations, and emotions to remission, striking a balance between a desire for normalcy and the risk of recurrence; arrange for an appropriate community agency to monitor the patient/family situation and provide support and counsel.

4. Persistent or Recurrent Disease

Patient-Family Task. Accept life-style changes, including patient's relinquishment of cherished roles; working through feelings of hopelessness and also volatile family emotions arising from the tension between adjustment needs and family values, goals, and satisfactions; redistribution of family obligations to remove strain and minimize feelings of competition among family members.

The Social Work Focus. Help the patient exercise choice, where possible; accept helplessness and dependency, where necessary; minimize excessive emotional regression and discourage desperation and recourse to expensive "magical" cures which lack scientific validation; help the family to work through anger, guilt, and helplessness and adjust their values, goals, and satisfactions; foster co-operation and mutual support among family members.

5. Terminal Illness

Patient-Family Task. Grapple with fear, anguish, and fantasy about the mode of death; learn to use medical and internal resources to minimize pain, while retaining as much self-sufficiency and personal dignity as possible; accept that life is time-limited.

The Social Work Focus. Help patient and family through anticipatory grief; foster intimacy among family members; help patient and family to separate from each other, where either may so desire; provide patient and family with resource counselling and advocacy; provide psychotherapy to resolve conflicts outside the cancer issue.

6. Death and Bereavement

Patient-Family Task. Grieve their loss by working through feelings of guilt, self-absorption, and alienation; reorienting their lives.

The Social Work Focus. Bereavement counselling to give relief from guilt, alienation, emotional intensity, and self-absorption.

A COMMUNITY CANCER OUTREACH PROGRAM

S. MARKLAND*, *London, Ontario*

In 1987, the London Regional Cancer Centre (LRCC) initiated a regional education program in primary, secondary and tertiary prevention—formerly called Oncology Education—it now has a new title, Community Cancer Outreach Program, which more accurately reflects the key underlying principle of community-based collaboration. Specifically, the program recognizes the need to establish strong partnerships with diverse cancer-interest groups in Southwestern Ontario. The network, which has been established over the past three years, includes professionals in health care and education, volunteers of the Canadian Cancer Society (CCS), and the collective membership of numerous community service and church-affiliated groups.

The collaborative approach to prevention education has several important advantages. First, it fosters a shared sense of ownership and commitment to the challenge of reducing cancer incidence, morbidity and mortality in the region. Secondly, it minimizes the duplication of resources, allowing a more cost-effective dissemination of consistent messages that transcend "turf" boundaries. Thirdly, a coalition of cancer interest groups attracts greater external funding and media support. Fourthly, given that prevention initiatives often are conceived, planned or conducted jointly on the basis of identified needs, target audience response is uniformly positive. Finally, regional networking broadens program scope and impact even with a staff initially limited to one full-time position during its formative stages. There are now three full-time positions; a fourth will be added early in 1991.

Tertiary Prevention

Although the Outreach Program is active in primary and secondary prevention, this discussion will focus on the tertiary level of activity and its links with the regional network. The American Cancer Society describes tertiary prevention as the identification and modification of the psychological, social, economic and physical effects often associated with the diagnosis, treatment, rehabilitation and continuing care of cancer patients and their significant others. Given the size of the LRCC's catchment region—

---

* Director, Community Cancer Outreach Program, London Regional Cancer Centre.

11 counties with a total population of 1.3 million, and 105,000 new and follow-up cases projected for 1990—the program focuses on the development, co-ordination and promotion of information and resource exchange. We consider that it is equally important to remove geographic, logistic or systemic barriers to information and resources.

The Program stands at the interface between community and treatment centre, where gaps in care and strategies to close them are more readily identified. The Program's emphasis on networking to equalize the quality and quantity of care across LRCC's catchment area views the patient and family as consumers of service, rather than passive recipients of a regional cancer-care system. Thus, a fundamental program goal is to empower the patient and family, thereby increasing their ability to influence the decision-making process. Simply stated, we enlist the network's participation in offering the right information to the right people at the right time; we determine the "rightness quotient" on the basis of solicited consumer needs and opinions. The following description of prevention strategies illustrates how we have applied the principles of collaboration and consumerism to expand the Program across all spheres of prevention.

Patient and Family Library

The Patient and Family Library was opened following a pretested survey of the cancer information needs of 285 patients and their families (Table I). We used the results to guide selection of books, pamphlets and videos, which are being supplemented by donations from patients and pharmaceutical companies.

The Library is staffed by 12 volunteers, who were recruited by the CCS and wear the traditional yellow smocks, but were trained by and are accountable to the Outreach Program. CCS patient education material is used extensively in the Library, and there is a designated telephone hookup to the toll-free provincial Cancer Information Service.

Volunteer staff have been trained in listening skills and familiarized with LRCC and regional support services in response to some patients' and family members' tendency to disclose concerns about illness and treatment during Library visits. Attentive volunteers have made several referrals to departments such as social work and nutrition, and have informed patients of services and resources available in their home communities.

Video Series

Via the regional network, patient and professional education videos have conveyed cancer information to significant numbers of viewers (Table II). Each has been professionally produced and funded by a pharmaceutical company. Their brevity (<15 minutes), focus on multidisciplinary care, and the use of patients and families as "actors" and script reviewers make this approach effective with both patients and professionals.

Under the combined direction of a patient advisory group and a film production company, we are preparing a television documentary, which will examine the diagnosis and treatment of cancer as it affects the physical and psychological health of women at home and work. This documentary, for which we are seeking funding from the National Film Board, arose out of two public events in 1990, both entitled "Looking Good, Feeling Better", which drew many women at various stages of illness and treatment. These events focused on five women with cancer who selected and modelled practical, low- to mid-price clothing aimed at reducing discomfort during post-surgical and active stages of treatment. LRCC staff also gave brief presentations on skin and hair care, nutrition and exercise needs of cancer patients, supported by related product displays and donations of goods or services by local retailers. This program will be conducted annually, in response to strong public and media endorsement of its approach to bringing cancer issues "out of the closet" and normalizing the impact of this disease on quality of life.

Conferences

To date, one-day conferences held at LRCC or in the community have attracted more than 1700 healthcare professionals and CCS volunteers. These meetings identify problems in regional delivery of cancer care, which vary among communities according to the level, type and availability of cancer-care resources. Frequently, these meetings also provide solutions to specific problems, and both referrals and consultations have increased, particularly with respect to nursing, social work, nutrition and palliative care. Often these conferences are held in the community, but those that are held at LRCC allow regional cancer-care providers to observe, first-hand, multidisciplinary treatment approaches, clarify misconceptions or to resolve communication problems through personal contact with LRCC staff.

In addition, we jointly plan and conduct separate, fully subscribed conferences with individual units of the CCS, to disseminate accurate, current cancer information to patients and families in rural communities and small towns.

ONCORE

This quarterly publication links the oncologist and primary-care physician with concise, pragmatic information on cancer prevention, early detection, multidisciplinary treatment and research. The five issues of *ONCORE* published since October 1989 have been funded by Purdue Frederick, Inc., and distributed to 9000 physicians in Canada. Of these, 2300 physicians and other healthcare professionals in LRCC's catchment region and elsewhere in Ontario receive copies by mail, and the remainder are distributed by Purdue Frederick. *ONCORE* is deposited with the National Library of Canada and the British Library, and its circulation continues to increase. We are evaluating its effectiveness as a "bridge" between the community and treatment centre by means of a large readership survey.

Public Lectures

An evening lecture series held at the LRCC on tertiary prevention for patients and their families drew only 20 individuals, whereas two annual lecture series on prevention and treatment drew a combined public, patient and family audience of 1250. By the end of the series, those who attended the former had evolved into a cohesive support group whose participants openly shared thoughts and feelings about quality of life issues. Assuming that the choice of information and audience were correct in each case, we might explain the disparity in response between the patient and the public lectures by the timing of presentation. Patients—particularly those from out-of-town—seem unable or unwilling to attend evening information sessions, however relevant to need. In planning a second series, we will take into account external or personal barriers to attendance by patients who are disabled by treatment.

Cancer Information Telephone Service

In our area, direct access to cancer prevention information is available through the Outreach Program's public enquiry line, which is listed in the London telephone directory. Between 1989 and 1990, the program received 85 calls from individuals seeking information on a wide variety of prevention, treatment and disease-related issues. Typically, callers are distraught, unaware of cancer resources in their community, lack basic information about their type of cancer, and require practical guidance how to access the necessary services and resources. As a rule, we refer callers to the provincial hotline, and we sent them appropriate CCS education materials. We also encourage them to use the Patient and Family Library, and above all, to consult their family physician for advice and direction.

In conclusion, this outline of tertiary prevention strategies illustrates the Community Cancer Outreach Program's dependence on the regional network. It underscores the degree to which continuing dialogue with target groups helps maintain the Program's relevance and credibility. Indeed, the entire process of tertiary prevention education is one of dynamic, responsive and adaptive interaction with patients, families, volunteers and professionals, who collectively share the benefits of this united effort to improve cancer care in Southwestern Ontario.

TABLE I

PATIENT AND FAMILY LIBRARY JUNE-DECEMBER 1990

Female patients/relatives	1060
Male patients/relatives	477
Staff	254
TOTAL	1791
Contents of Library	
Books	305
Videos	20
Audiocassettes	20
Pamphlet rack topics	62
Reference file	–

Most Frequently Requested Subjects

1. Coping With Cancer
2. Relaxation therapy
3. Treatment issues
4. Self-help
5. General information (pamphlets, reference books)

TABLE II

VIDEO DISTRIBUTION

Title	Circulation	Target Audience
Ray Of Hope, 1990	41	Patient/Family
Understanding Radiation Therapy, 1987	64	Patient/Family
Understanding Chemotherapy, 1988	68	Patient/Family
Coping With Cancer, 1989	74	Patient/Family
You're In Control (Nutrition) 1991	7	Patient/Family
Management of Cancer Pain, 1990	59	Professional
Palliative Care, 1990	74	Professional
TOTAL	387	

RESEARCH IN COPING INTERVENTIONS

S. SELLICK, Ph.D.*, *Thunder Bay, Ontario*

Psychosocial oncology is a rapidly growing area of clinical and research activity, that is shared by a number of health-care professionals. Society has long recognized that, in addition to physical needs, the patient has the considerable need for attention to the mind and spirit. In the last 15 years psychologists, for example, have demonstrated a growing interest in physical disorders, initiated in part by the report of an American Psychological Association Task Force, which studied psychology's role in health research. The report stated in part that:

> There is probably no specialty field within psychology that cannot contribute to the discovery of behavioral variables crucial to a full understanding of susceptibility to physical illness, adaptation of such illness, and prophylactically motivated behaviors[1].

Behavioral research in oncology falls logically into three broad but not exclusive areas of interest:

1. Are some individuals more susceptible than others to cancer, and can we identify psychological characteristics, which might help us to identify and predict an individual's risk factors?
2. Are there identifiable influences, which the mind can exercise, that will increase the likelihood of recovery; what are the mechanisms by which such healing might take place?
3. What adaptations must one make to minimize psychological morbidity and enhance quality of life?

Let us acknowledge that people do the best they can by using what, for them, has been their preferred method of coping though it can be improved upon. In addition, while most people will be open to suggestions, in some, old habits linger, and they prefer the security of old coping strategies.

As a generalization, it appears that psychologists provide information, which will encourage an attitude of responsibility for making the best of a bad situation, and impart skills for mastering one's emotions, attitudes, and behaviors. They may, for example, seek to reinforce a cluster of character traits termed "hardiness"[2] which, along with exercise and social support, appear to protect against illness. Individuals with hardy personalities have a strong sense of control, a sense that they can influence events in their own lives; they have a high degree of commitment to people, activities, and events in their lives; and such people view change as a challenge, an opportunity for growth. All other things being equal, the hardy individual is less likely to become ill when faced with stress. Individuals, who experience high levels of stress and do not cope well (are not "hardy"), show poor immune system activity[3,4]. At this point we might assume that if one is to fare well, one must learn all there is to know about the disease, adopt a fighting spirit, and cultivate an atmosphere of positive expectation. However, as yet, we cannot make consistent predictions about what will happen to those who follow such advice, as opposed to those who do not.

---

*Director, Department of Psychosocial Services, OCTRF Thunder Bay Regional Cancer Centre; and Adjunct Professor and Sessional Lecturer, Lakehead University, Thunder Bay.

Most cancer patients show a remarkable degree of resilience and adapt well[5]. Among hospitalized cancer patients, less than one-half show significant emotional difficulties, and most of these respond to psychological therapy[6]. For example, Craig, Comstock, & Geiser[7] surveyed 130 breast cancer patients who were assessed at least nine months after diagnosis, and 260 women from the general population. The two groups did not differ in measures of depression, happiness, optimism for the future, or perceived health.

Coping programs have long been available. The Canadian Cancer Society offers a number of individual and group supportive care programs and Dr. A. Cunningham (Ontario Cancer Institute) has facilitated cancer coping courses for a number of years. The eight Cancer Treatment Centres have psychologists and/or social workers available to patients and families for information, assistance, supportive counselling, and psychotherapy.

At the Thunder Bay Regional Cancer Centre (TBRCC), we have conducted a pilot study with 20 chemotherapy patients, one-half of whom listened daily to a relaxation/guided visualization audiotape, and one-half of whom listened to a music tape of equivalent length. Over a six-week period, both groups demonstrated a similar decrease in anxiety (state and trait) and an increase in quality of life. Some patients prefer to listen daily to relaxation music rather than to a therapist describing images that may aid the patient to cope with treatment side-effects or combat the disease itself[8]. These results remind us that we can convey a sense of concern and support in a number of ways...the actual technique may not be important. It may be beneficial to take time out every day to do what you need to do, but what or who you listen to may not be crucial.

In another study at the TBRCC, 60 patients completed several questionnaires before their scheduled follow-up visits, and were interviewed on the day of their appointment. One measure assessed the patient's notion of how much control (over health matters) was in his or her hands as opposed to being in the hands of others (i.e., medical personnel), or was simply due to chance. This study suggests that a strong belief in one's own control was associated with high stress; those who reported relatively low daily stress also believed that control belonged to others, or to chance. A second measure asked how much control each patient desired. Again the responses suggest that those who scored high on desirability of control also scored high on daily stress. It appears that for some cancer patients, not having control and not wanting control is beneficial; that adopting an attitude of quiet acceptance may be a useful coping strategy. These are the people who don't read the self-help books given to them by well-meaning family and friends. To leave power and control in the hands of others frees the patient to live life. Matters pertaining to the illness are left to the experts or to chance.

Patients employ numerous strategies in an effort to cope with cancer and undoubtedly the meaning of the diagnosis is different for each patient. It is crucial that each caregiver match his/her style of caring to the individual patient's style of coping. Each of us has a schema, which is useful to us because it helps order our world and create a sense of predictability and stability. Patients with chronic illnesses will have at least one of a number of such maps, depending on their beliefs about whether the illness is their fault or not, and whether they are responsible for restoring their bodies to health, or whether this task belongs to the physician[9].

Caregivers often attempt to identify types of patients in order to create a sense of order, and label patients accordingly. We will care best for these people if we see each of them in the context in which they find themselves, in the relationships they have with the people around them. A patient's ability to cope is a reflection of the relationship that person has with family and friends, and with professional caregivers. For some, meeting regularly with other cancer patients may prove to be beneficial. Spiegel, Bloom, Kraemer, and Gottheil[10] demonstrated that survival time was significantly longer in patients with metastatic breast cancer if they had participated for one year in a support group that met weekly, compared to a control group who had not had such a program. Here it is tempting to assume that the active ingredient in the prolonged survival was the weekly meeting. However, we must be careful to ensure that we do not begin to look merely for the best way to cope. Some authors have argued that the first step in rising above the illness is to accept responsibility for having the disease in the first place. As untenable as this may be, many people seem to hold dearly to this notion, because in accepting responsibility these people find hope. If one had a part to play in the creation of the condition, perhaps one can exercise control in its cure.

There is no shortage of material about the importance and potentially crucial impact that one's mental attitude may have on one's quality of life and upon long-term survival. It is at this point, however, that we lose consensus regarding the influence of psyche upon cancer. We understand little about the mechanisms by which the influence of social support groups, for example, might bring about remission and a longer life, and we need to replicate these studies. We need to identify the key ingredients and assess the various components of successful programs. We need to spend more time talking with and listening to patients, learning from them, about what it is that makes a difference to them, to their sense of well-being, and to the quality of their lives. Our support programs must become their programs, designed and evaluated by patients and caregivers working together; we must be ever mindful that the most important and only useful theory about what will help will be found, not in a text or journal, but within the individual patient…it will be the patient's theory. Then our task will be to match our practice to the theory and tailor our caregiving to the needs and coping styles of that individual.

The OCTRF employs or contracts psychologists in three centres—Sudbury, Thunder Bay, Toronto-Bayview. These psychologists have formed an informal collaborative and supportive network, the Psychologists' Research Group in Oncology (PRGO). As more centres bring psychologists on staff, the potential for multicentre studies will grow. Many questions clamor to be asked, questions about the needs of patients, the coping styles preferred by different types of patients with different types of concerns, and the impact of psychological intervention upon the individual's quality of life, and upon his/her long-term survival. I hope more centres will recruit psychologists to their staff so that, collaborating with one another and with colleagues in other disciplines, we can get on with the challenging work before us.

REFERENCES:

1. American Psychological Association. Task Force on Health Research. Contribution of psychology to health research: Patterns, problems, and potential. *Am Psychol* 1976; **31:** 272.
2. Kobasa SCO, Maddi SR, Pucetti MC, Zola MA: Effectiveness of hardiness, exercise and social support as resources against illness. *J Psychosom Res* 1985; **29:** 525.
3. Kiecolt-Glaser K, Glaser R: Psychological influences on immunity. *Psychosomatics* 1986; **27:** 621.
4. Levy SM: Behavior and Cancer. San Francisco: Jossey-Bass, 1985
5. Sarafino EP: Health Psychology: Biopsychosocial Interactions. Toronto: John Wiley & Sons, Inc. 1990: 460.
6. Burish TG, Meyerowitz BE, Carey MP, Morrow GR: The stressful effects of cancer in adults. *In:* Baum A, Singer JE, eds. Handbook of Psychology and Health, vol. 5. New York: Erlbaum, 1987.
7. Craig TG, Comstock GW, Geiser PB: The quality of survival in breast cancer: A case-control comparison. *Cancer* 1974; **33:** 1451.
8. Straw G, Sellick MA, Sellick SM: The use of relaxation and guided mental imagery for the quality of life of cancer patients. *Can Psychol* 1990; **31(2a):** 413.
9. Northouse LL, Wortman CB: Models of helping and coping in cancer care. *Patient Educ Couns* 1990; **15:** 49.
10. Spiegel D, Bloom JR, Kraemer HC, Gottheil: Effect of psychosocial treatment on survival of patients with metastatic breast cancer. *Lancet* 1989; **2:** 888.

PSYCHOSOCIAL AND PALLIATIVE CARE AT THE HAMILTON REGIONAL CANCER CENTRE

Dr. David Ginsburg's 1989 report entitled "Supportive Care of Patients With Malignant Diseases in the Ontario Regional Cancer Centres" generated a great deal of discussion at the Hamilton Regional Cancer Centre (HRCC). Because our current methods of treatment demonstrate disappointing plateaus in survival curves for many cancer sites, provision of excellent supportive care becomes a major challenge. As the cure and care continuums converge, we need more than ever before a responsive and comprehensive cancer care system.

Over the past decade at the HRCC, supportive care has been provided to patients and families by primary nurse-physician teams in interdisciplinary clinics, by radiation therapy technologists and oncology nurses during treatment and by Canadian Cancer Society volunteers through their numerous programs. In the presence of overwhelming distress, the psychosocial team offers psychiatric consultation, behavioral training, relaxation techniques, bereavement counselling and social work support. In 1990, a "Music for Wellness" project was initiated as a joint nursing project with our host hospital. Our patients now have available an impressive repertoire of audiotapes to listen to during treatments or when they are admitted to the Henderson General Hospital.

The Symptom Control Clinic provides in-depth consultations regarding management of complex symptoms and palliative care. Patients and HRCC staff have access to the clinical associates, oncology nurses, pharmacists, radiation and medical oncologists, radiation therapy technologists and a social worker. Throughout the week such care is co-ordinated by our nurse co-ordinator, Marilyn Miscione, in collaboration with HRCC primary teams and various community health care providers.

In March 1990, the Nursing Department conducted an interdisciplinary audit on 75 charts to study the documentation of the supportive care, provided to patients and families. The observers collected data on 22 high-incidence problem areas directly caused by cancer or its treatment. They identified gaps in documentation and presented the data at a clinical trials dinner meeting in March 1990. A high level of interest was generated and, within two months, the Senior Management Advisory Committee established the Ad Hoc Supportive Cancer Care Working Group. This group, which consists of nine members from a variety of health disciplines, is chaired by June Scruton, Acting Senior Nurse Administrator. Its mandate is to develop a proposal for a clinical supportive cancer-care program. The group has completed a comprehensive literature search, has initiated a needs assessment and is conducting interviews with key informants.

Concurrently our Senior Nurse Researcher, Ann Mohide, who was recruited in May 1990, is preparing an application for a Health System Linked Research Unit to the Ontario Ministry of Health. The proposal for a Supportive Cancer Care Research Unit (SCCRU) is sponsored by McMaster University, Faculty of Health Sciences in partnership with the Hamilton and Thunder Bay Regional Cancer Centres and the Metro Hamilton and Northwestern Districts of the Canadian Society. The proposal defines supportive cancer care as "those health services and related activities designed to help patients and families with their cancer experience during the diagnostic treatment (radiation, chemotherapy, surgery or a combination thereof) and follow-up phases".

The SCCRU's overall goal is to improve the supportive health services and related activities provided to cancer patients and their families. Using a needs, resources and services framework, an interprofessional team of eight investigators will conduct research in four areas: Information exchange, roles and needs of informal caregivers, identification of high-risk groups and evaluation of supportive care strategies, and issues of survivorship. Together, these themes cover supportive care issues arising throughout all phases of cancer management. The studies will emphasize ambulatory, community and home-based delivery of supportive care, and, in addition, the means of strengthening the collaborative and complementary roles of the formal and informal resource sectors. The SCCRU will assist in the direct application of its research findings by developing and disseminating implementation guidelines and quality-assurance packages to accompany the guidelines. Research productivity will be facilitated through collaborative research, the development of research capabilities of interested health professionals, and graduate-student research experience.

The HRCC sponsored a supportive cancer care planning retreat on January 30, 1991. Participants included members of our Senior Management Advisory Committee, the Ad Hoc Supportive Cancer Care Working Group, the investigators of the proposed SCCRU and our colleagues from the community and host hospital. This initial dialogue and a firm commitment to the development of strategic alliances will speed the evolution of a responsive supportive cancer care network in Central-West Ontario.

In spite of the accelerating pace of planning for our new centre and the implementation of OPIS before Christmas, our staff are committed to a vision of comprehensive cancer care, which integrates supportive care as an essential component of all that we do at HRCC.

June Scruton, R.N.
Acting Senior Nurse Administrator

SUPPORTIVE CARE INITIATIVES AT THE KINGSTON REGIONAL CANCER CENTRE

We have enhanced patient care considerably by the appointment of a social worker, Donna Forster, and she has instituted a number of groups already; a senior psychiatry resident, Dr. George Linn, rotates through the Centre on a full-time basis; the presence in the Centre of a home care co-ordinator, Jackie Dickenson, has improved the integration of the Centre's home care functions; finally we have organized biweekly "psychosocial rounds" for the Centre's staff, hospital and community nurses, social workers, clergy, technologists, pharmacists and physicians.

Our nurses now phone all new referrals to the Centre before their appointments and orient them concerning the first visit; we hope this will reduce the anxiety and stress of visiting a cancer centre for the first time. These patients are met and assessed by the nurse, who telephoned them. This same nurse participates in the physician's initial assessment and in the discussion with the patient and the family of subsequent investigation and management.

Dr. Bill Mackillop, Carol Quirt and Dr. Lynne Ginsburg (Psychiatry) are interviewing patients with lung cancer to assess their understanding of the illness and its therapy, and to determine its relationship to mood. We are strengthening our links with the Department of Psychology at Queen's University (Dr. Julian Barling); for example, a recent M.Sc. thesis by Wendy Stewart was concerned with the effects of stress on performance by nurses, technologists and physicians.

In June 1990, we held a successful two-day symposium on supportive care; it included presentations by the Centre, Queen's University and hospital faculty and by two distinguished guests, Mary Vachon and Barrie Cassileth. Wendy Stewart and her committee, are arranging the 1992 Canadian Association of Psychosocial Oncology Conference, which will be held in Kingston.

A.D. Ginsburg, M.D.
Chief Executive Officer

DEPARTMENT OF PSYCHOSOCIAL SERVICES AT THE THUNDER BAY REGIONAL CANCER CENTRE

Dr. Scott Sellick, psychologist, and Ms. Heather Neilson, social worker, provide supportive care services to cancer patients and their families, and co-ordinate available resources within the community and in other parts of the province. The Thunder Bay Regional Cancer Centre (TBRCC) has been accepting therapy referrals from other centres and this has demanded considerable social work time, in making travel arrangements and tending to the needs of these out-of-town patients.

The Department of Psychosocial Services is a relatively new addition to the TBRCC. The psychologist joined the Centre in the fall of 1988 and the part-time social worker was recruited early in 1990. Because each is affiliated with their respective faculties at Lakehead University, undergraduate social work and graduate psychology students are receiving practicum experience at the TBRCC. The students have spoken well of the experience and it has proven to be most beneficial to the Centre as well. The social work student has gathered information for the design of a patient resource centre, and the psychology graduates have been involved in the psychologist's ongoing research.

The psychosocial oncology research program has completed a number of pilot projects which now are being considered as a basis for larger studies; we are seeking outside funding for these. These projects have been the subject of theses research undertaken by students completing the requirements of the M.A. in clinical psychology; they are supervised by the Centre's psychologist and by a faculty member from Lakehead University. These themes have included:

- The experience of staff working in a cancer care facility—burnout and job satisfaction.
- The impact of two different psychological interventions for chemotherapy patients—what are the active ingredients necessary for the maintaining of one's quality of life?
- The cancer patient's experience of follow-up visits—what is the extent of any psychological morbidity created by the visit, and for whom are these visits most beneficial, emotionally?
- Medication compliance among breast cancer patients who have been prescribed tamoxifen as adjuvant therapy, and among women with metastatic disease.

These projects have been presented at the annual meetings of the Canadian Association of Psychosocial Oncology, the Canadian Guidance and Counselling Association, and the Canadian Psychological Association.

The Department hopes to increase its staff and expand its programs. It is seeking funding for a part-time pastoral care worker and for a one-year doctoral internship position in health psychology.

S. Sellick, Ph.D.
Clinical Psychologist

PSYCHOSOCIAL AND PALLIATIVE CARE FOR PATIENTS WITH CANCER AT THE WINDSOR REGIONAL CANCER CENTRE

Since the last provincial survey two years ago psychosocial and palliative care services at the Windsor Regional Cancer Centre has improved but, due to space and resource limitations, these services are still inadequate.

Social service at the Windsor Centre is provided mainly through the Victorian Order of Nurses (VON) staff. For the past two years, two VONs have operated in close liaison with the attending staff in the departments of radiation and medical oncology. The VONs, who are seconded to the Centre from the VON office in the city, are designated as community liaison nurses. They report to the Assistant Director of VON and are responsible to the Chief Operating Officer of the Centre. They are paid through the VON who, in turn, are reimbursed through the Centre's budget. Their primary function is as the need arises to link the Centre's patients to appropriate community social services such as home care, public health and hospice. Through other agencies in the city, they also provide counselling concerning nutrition or financial assistance. Within the Centre, the VONs attend the weekly departmental meetings to report on the progress of patients and also to receive new instructions concerning the need for home care. Acting together the oncologists, clinic nurses and VONs provide some psychology services on an ad hoc basis.

During the past year, a third VON has been added as a home care coordinator and has an office in the Centre. This additional service is provided at no extra cost to the Centre.

The Chaplain in our host hospital provides pastoral care for inpatients.

The Hospice of Windsor has a fairly well developed community service. It has a close tie to the Centre and most of their clients are cancer patients. The Hospice has a large group of trained volunteers, three full-time and four part-time RNs, a pastoral care service and two psychologists. Their nurses attend the weekly medical oncology rounds and also act as patient advocates for palliative care. The psychologists provide their services on a referral basis. The Hospice also accepts patients with other diseases such as AIDS.

Windsor does not have a separate palliative care unit but the oncologists provide symptom control, particularly the relief of pain.

We hope to establish a formal psychosocial service department with the next renovation and the expected increase in clinic space.

G.C.K. Mok, M.D.
Chief Executive Officer

EDUCATION

SUMMARY OF OCTRF EDUCATION ACTIVITIES

Postgraduate Medical Education

In 1990 the Foundation continued its support of postgraduate medical education by funding 16 residencies in oncology (medical and radiation) at a cost of approximately $750,000. The residency posts, which supplement those funded by the Ministry of Health in the five medical schools in the province, are an attempt to relieve the serious manpower shortage in these specialties.

Undergraduate Medical Education

The Ivan H. Smith Memorial Studentships

This program, jointly funded by the Canadian Cancer Society Ontario Division and the Foundation, provided 20 studentships (18 adult; 2 pediatric) in 1990 for periods of from 4 to 12 weeks. Competition for studentships is open to medical students after their second year of study. Studentships in adult oncology are offered at the OCTRF Regional Cancer Centres and the Princess Margaret Hospital, while pediatric oncology studentships can be held in facilities at The Hospital for Sick Children (Toronto), The Children's Hospital of Eastern Ontario (Ottawa), The Hotel Dieu Hospital (Kingston), The Children's Hospital of Western Ontario (London), and the McMaster University Medical Centre (Hamilton). Named in honor of the late Dr. Ivan H. Smith, an internationally known radiation oncologist, Professor of Radiation Oncology at The University of Western Ontario and Director of the London Regional Cancer Centre, the Ivan Smith Studentships introduce medical students to the rewarding aspects of a career in oncology.

The Harold E. Johns Summer Studentships in Medical Physics

In 1990, 12 studentships were taken in the following centres: Hamilton, Kingston, London, Ottawa, Thunder Bay, Toronto-Bayview and the Princess Margaret Hospital. This program, which is intended to stimulate the entry of medical physicists into oncology, is funded from a special cancer services improvement grant from the Canadian Cancer Society Ontario Division.

Continuing Medical Education

In 1990, staff members supported clinic days, seminars and guest lectures in the OCTRF Regional Cancer Centres and the Princess Margaret Hospital and gave lectures in the community.

During 1990, the Cancer Information Service (CIS) continued to serve cancer patients, their families and friends, the public, the media and health professionals across the entire province. This service is sited in Hamilton near the regional cancer centre and is jointly supported by the Foundation and the Ontario Division of the Canadian Cancer Society. In April 1990, the CIS underwent an on-site review by two Canadian and two American experts. The site visitors concluded that the CIS was providing a high-quality service. They recommended an aggressive promotion of the CIS and the development of a new series of services; e.g., health promotion and screening initiatives, an exchange of information on referrals to clinical trials and institutions and a consultation network linking health professionals outside the Foundation with health professionals within OCTRF.

The 1990 visitor to Israel selected under the Joseph J. Schiffer Exchange Program was Dr. Ronald Feld. His visit is expected to take place during early 1991, but the exact date has yet to be confirmed. This program, sponsored jointly by Mount Sinai Hospital and the Foundation, promotes scientific interchange between Israel and the University of Toronto health sciences facilities by supporting annual exchange visits of individuals working in the field of cancer care and/or research.

The 1990 W. G. Cosbie Lecture was presented by Dr. James H. Goldie of the Cancer Control Agency of British Columbia at the 14th Annual Meeting of the Canadian Oncology Society held in Toronto in September.

In October 1990 the OCTRF Lecture, entitled "The Application of DNA Analysis by Flow Cytometry to Human Solid Tumors", was delivered by Dr. John D. Crissman, Professor of Pathology, Wayne State University (Detroit), at the 53rd Annual Meeting of the Ontario Association of Pathologists in Windsor.

Dr. Denis P. Burkitt, discoverer of Burkitt's lymphoma and the role of dietary fibre, presented the 1990 Gordon Richards Memorial Lecture. Dr. Burkitt presented his talk, entitled "Winning the War on Cancer", at The Princess Margaret Hospital on November 26, 1990.

The Ontario Cancer Treatment and Research Foundation/Canadian Cancer Society Ontario Division Joint Advisory Group on Education

During 1990, representatives from the Ontario Division of the Canadian Cancer Society and from the Foundation met to discuss their respective activities in public, patient and health professional education. Presently, this group is developing an educational plan which it is hoped will avoid undue duplication and lead to a number of joint ventures.

J. C. Laidlaw, M.D., Ph.D., FRCPC

12TH CLINICAL CANCER RESEARCH CONFERENCE
GENEVA PARK, LAKE COUCHICHING, ONTARIO

From April 22 to 24, 1990 approximately 150 members of the Ontario Cancer Treatment and Research Foundation (OCTRF) attended the 12th Clinical Cancer Research Conference at Lake Couchiching, Geneva Park, Ontario. The medical and radiation oncologists, career scientists and medical physicists enjoyed the conference and the spring scenery of Lake Couchiching. All previous conferences had been held every second year in the fall, however, due to scheduling conflicts the 12th conference was postponed from Fall 1989 to Spring 1990.

"Molecular Biology of Cancer" was chosen as the theme of the conference for two reasons. First, major advances in the field of molecular biology, particularly in cancer research had been achieved in the previous 10 years and subsequently substantial knowledge had been acquired about the biology of cancer over this same period. Second, some of the knowledge obtained at the bench was being applied at the bedside in clinical oncology practice.

The Ottawa Regional Cancer Centre (ORCC) was responsible for selecting the conference theme and speakers. Many members of the ORCC assisted the five committee members—Drs. Birnboim, Danjoux, Evans, Logan (Chairman) and Raaphorst.

The program had two plenary sessions, a poster session and a keynote OCTRF Research Lecture. The keynote OCTRF Research Lecturer was Dr. I.B. Weinstein (Director, Comprehensive Cancer Center, Columbia University, New York, NY), who presented "The Molecular Biology of Cancer"*. Members of the ensuing panel discussion were Dr. M. Paterson (Cross Cancer Institute, Edmonton, Alberta), Dr. R. Phillips (Hospital for Sick Children, Toronto) and Dr. C. Birnboim (Ottawa Regional Cancer Centre).

The first plenary session entitled "The Role of Oncogenes in Malignancy and the Clinic" was co-chaired by Drs. Birnboim and Logan. The five presentations were: "An Overview of Molecular Biology and Techniques"* by Dr. R. Hawley (Ottawa Regional Cancer Centre); "The Role of Transgenic Mice in Clinical Cancer"* by Dr. N. Lassam (Toronto-Bayview Regional Cancer Centre); "The Molecular Biology of Atazia-Telangiectasia" and "The Role of the *Neu* Oncogene in Breast Cancer"* by Dr. M. Paterson (Cross Cancer Institute, Edmonton, Alberta); "Oncogenes and Chromosomal Translocations—Their Clinical Exploitations in Malignant Lymphoma"* by Dr. N. Berinstein (Toronto-

Bayview Regional Cancer Centre) and "Anti-Oncogenes"* by Dr. R. Phillips (Hospital for Sick Children, Toronto).

The second plenary session, "Molecular Basis of Resistance in Malignant Cells", was co-chaired by Drs. P. Raaphorst and D. Stewart. The three speakers for this session were Dr. R. Weichselbaum (Department of Radiation and Cellular Oncology, University of Chicago Center for Radiation Therapy, Chicago, Illinois), who discussed the "DNA Basis of Radiation Sensitivity"; Dr. J. Koropatnick (London Regional Cancer Centre), who presented "Metallothionein and Cell Resistance"* and Dr. J. Gerlach (Kingston Regional Cancer Centre), who reviewed "Mechanisms of Cell Drug Resistance".

Finally, the poster session for this conference was held in a new format with poster displays and six simultaneous forums for verbal presentation and group discussion to enhance exchanges between researchers with similar research foci. The six themes were: "Biology of Cancer" (Chair, Dr. R. Liteplo, Ottawa Regional Cancer Centre); "Cancer Biology and Molecular Biology" (Chair, Dr. C. Birnboim, Ottawa Regional Cancer Centre); "Clinical Oncology—Therapeutic Trials" (Chair, Dr. J. Maroun, Ottawa Regional Cancer Centre); "Cancer Biology, Growth Factors and Receptors" (Chair, Dr. D. Logan, Ottawa Regional Cancer Centre); "Medical Physics" (Chair, Dr. P. Raaphorst, Ottawa Regional Cancer Centre); and "Clinical Oncology—Epidemiology and the Health Care System" (Chair, Dr. C. Danjoux, Ottawa Regional Cancer Centre).

D. Logan, M.D.
Conference Chair

---

*Copies of the papers marked with an asterisk are available on request from:
The Editor
The Ontario Cancer Treatment and Research Foundation
7 Overlea Blvd.
Toronto, Ontario
M4H 1A8
Canada

SUMMARY OF THE 26TH OCTRF CLINICAL CONFERENCE: LUNG CANCER IN THE 1990s

On November 2, 1990, the Northeastern Ontario Regional Cancer Centre in Sudbury hosted the 26th OCTRF Clinical Conference, at a time which coincided with the opening of the newest of the Foundation's regional cancer centres. Conference chairman was Dr. Robert E. Corringham.

The topic "Lung Cancer in the 1990s" was chosen because, compared to the rest of the province, Ontario's Northeastern Region has an excess mortality from lung cancer. In all of North America lung cancer continues to increase and to display a high ratio of mortality to incidence. Hence a major oncological challenge for the nineties remains the control of this cancer. The conference reviewed the magnitude of the problem, the current understanding of lung cancer and new strategies in prevention and therapy.

The 150 registrants represented all the regional cancer centres, the OCTRF Corporate Office, area physicians and nurses and representatives of pharmaceutical companies.

The first session, Epidemiology and Chemoprevention, was chaired by Dr. Eric Holowaty (Ontario Cancer Registry). Dr. Aileen Clarke (Division of Epidemiology and Statistics, OCTRF) examined the magnitude of the problem and options in prevention. Dr. Andrew Arnold (Hamilton Regional Cancer Centre) reviewed chemoprevention in lung cancer.

The second session, co-chaired by Dr. Glenwood Goss and Dr. William Evans (Ottawa Regional Cancer Centre), was devoted to Biology and Systemic Treatment. Topics covered were: Molecular Genetics of Lung Cancer, Dr. Adi F. Gazdar (National Cancer Institute, Bethesda, Maryland); IGF-I in Small-Cell Lung Cancer: Autocrine Growth Factor and Potential Treatment Target, Dr. Valentine Macaulay (Institute of Cancer Research, Sutton, U.K.); Dose Intensity in Lung Cancer, Dr. Wm. Hryniuk (Hamilton Regional Cancer Centre); Teniposide (VM 26) and Carboplatin as Initial Therapy for Small-Cell Lung Cancer, Dr. Glenwood Goss (Ottawa Regional Cancer Centre); Chronic Oral Etoposide in Small-Cell Lung Cancer, Dr. F. Anthony Greco (Vanderbilt University, Nashville, Tennessee); and Neoadjuvant Chemotherapy in Multimodality Treatment of Stage IIIA Non-Small Cell Lung Cancer, Dr. Arthur Skarin (Dana-Farber Cancer Institute, Boston, Massachusetts).

Dr. Randall Bissett (Northeastern Ontario Regional Cancer Centre) chaired the final session entitled Locoregional Therapy. The topics were: Photodynamic Therapy in Lung Cancer, Dr. Stephen Lam (British

Columbia Cancer Agency); High-Dose-Rate Endobronchial Radiotherapy for Carcinoma of the Lung, Dr. Clive Grafton (British Columbia Cancer Agency); The Role of Palliative and Curative Endobronchial Brachytherapy in Lung Cancer, Dr. Mark Schray (Emanuel Hospital, Portland, Oregon); The New Brachytherapy and its Application to the Treatment of Lung Cancer, Dr. Miles Mount (Nucletron Corp., Columbia, Maryland). Each session was followed by a panel discussion.

REGIONAL CANCER CENTRES

REGIONAL CANCER CENTRES

The Ontario Cancer Treatment and Research Foundation (OCTRF) was established in 1943 by an Act of the Ontario Legislature to conduct a program of research, diagnosis and treatment in cancer. The Foundation works in three fields: service, research and education. From its inception, the Foundation has accepted responsibility for:

- the establishment, maintenance and operation of research, diagnostic and treatment centres in general hospitals or special facilities; and
- the maintenance and operation hostels in connection with its treatment centres.

The Foundation also has the most important duty of co-ordinating facilities for cancer treatment and ensuring the adequate reporting of cases and the recording and compilation of data.

The Foundation with its eight Regional Cancer Centres—Hamilton, Kingston, London, Ottawa, Sudbury, Thunder Bay, Toronto-Bayview, and Windsor—provide facilities for undergraduate and postgraduate study, training of technical personnel, and research fellowships to increase our knowledge about cancer.

The Foundation is distinct from but co-operates with the Ontario Cancer Institute incorporating the Princess Margaret Hospital (OCI/PMH) in the investigation and treatment of cancer and works closely with the Canadian Cancer Society Ontario Division.

The Foundation hopes that *Cancer in Ontario* will assist the practising physician in some of the following ways:

- help him/her become familiar with the various services of the Foundation and its Centres;
- encourage effective patterns of referral and to promote efficient geographical use of the Regional Cancer Centres;
- encourage the individual physician to consult informally with staff members at the Regional Cancer Centres;
- make the resources of the Foundation more widely available to the people of Ontario by increasing the number of contacts between physicians, particularly those outside metropolitan areas, and the OCI/PMH and the Foundation's Regional Cancer Centres.

We urge any physician who reads *Cancer in Ontario* to make suggestions concerning the improvement of cancer control in Ontario. These may be transmitted to the Chief Executive Officer (CEO) of the nearest Regional Cancer Centre or sent directly to the President, Dr. J.W. Meakin. The CEOs of the Regional Cancer Centres, who also are Vice-Presidents (VPs) of the OCTRF, may be contacted as follows:

OCTRF Corporate Office
Dr. J.W. Meakin - President and Chief Executive Officer OCTRF
7 Overlea Blvd.
Toronto, Ontario M4H 1A8
Tel: (416)423-4240 FAX: (416)423-2017

Hamilton Regional Cancer Centre (HRCC)
Dr. W.H. Hryniuk - Chief Executive Officer HRCC and Vice-President OCTRF
Henderson General Hospital
711 Concession Street
Hamilton, Ontario L8V 1C3
Tel: (416)387-9495 FAX: (416)575-6323

Kingston Regional Cancer Centre (KRCC)
Dr. A.D. Ginsburg - Chief Executive Officer KRCC and Vice-President OCTRF
Kingston General Hospital
King Street West
Kingston, Ontario K7L 2V7
Tel: (613)544-2630 FAX: (613)544-9708

London Regional Cancer Centre (LRCC)
Dr. L. Levin - Chief Executive Officer LRCC and Vice-President OCTRF
Victoria Hospital
790 Commissioners Rd. E
London, Ontario N6A 4L6
Tel: (519)685-8600 FAX: (519)685-8614

Northeastern Ontario Regional Cancer Centre (NEORCC)
Dr. R.E.T. Corringham - Chief Executive Officer NEORCC and Vice-President OCTRF
Laurentian Hospital
41 Ramsey Lake Road
Sudbury, Ontario P3E 5J1
Tel: (705)522-6237 FAX: (705)523-7328

Ottawa Regional Cancer Centre (ORCC)
Dr. W.K. Evans - Chief Executive Officer ORCC and Vice-President OCTRF

Civic Hospital Division
190 Melrose Avenue
Ottawa, Ontario K1Y 4K7
Tel: (613)725-6300 FAX: (613)725-6320

General Hospital Division
501 Smyth Road
Ottawa, Ontario K1G 8L6
Tel: (613)737-7700 FAX: (613)737-6745

Thunder Bay Regional Cancer Centre (TBRCC)
Dr. J.F. Kotalik - Chief Executive Officer TBRCC and Vice-President OCTRF
General Hospital of Port Arthur
290 Munro Street
Thunder Bay, Ontario P7A 7T1
Tel: (807)343-1610 FAX: (807)345-2630

Toronto-Bayview Regional Cancer Centre (T-BRCC)
Dr. R.D.T. Jenkin - Chief Executive Officer T-BRCC and Vice-President OCTRF
Sunnybrook Health Science Centre
2075 Bayview Avenue
Toronto, Ontario M4N 3M5
Tel: (416)488-5801 FAX: (416)480-6002

Windsor Regional Cancer Centre (WRCC)
Dr. G.C.K. Mok - Chief Executive Officer WRCC and Vice-President OCTRF
Metropolitan General Hospital
2220 Kildare Road
Windsor, Ontario N8W 2X3
Tel: (519)253-5253 FAX: (519)971-9922

OCF

HAMILTON REGIONAL CANCER CENTRE

HENDERSON GENERAL HOSPITAL

Chief Executive Officer:

W.M. Hryniuk, M.D.

Radiation Oncologists:

V.R. Basrur, Ph.D., M.D.
D.I. Hodson, M.B., B.Ch.
C.R. Johanson, M.D.
G. Jones, M.D.
H. Lukka, M.B.,Ch.B.
W.D. Rider, M.B.,Ch.B.
J. Sathya, M.B.,B.S.
A.A.M. Tadros, M.B., B.Ch.
A. Whitton, M.B.,B.S.

Medical Oncologists:

A. Arnold, M.B.,B.S.
G.P. Browman, M.D.
E. Chouinard, M.D.
A.T. Figueredo, M.D.
M.N. Levine, M.D.
P.B. McCulloch, M.D.
A.J. Neville, M.B.,Ch.B.
J.J. Rusthoven, M.D.

Gynecologic Oncology:

G. O'Connell, M.D.
J. Mazurka, M.D.

Physicists:

C. Kwok, Ph.D.
C. Lewis, M.Sc.
M. Patterson, Ph.D.
V.G. Peters, B.Sc.
R.H. Price, B.Eng.
B.C. Wilson, Ph.D.
D. Wyman, Ph.D.

Clinical Assistants:

N. Frape, M.D.
H. Geffen, M.D.
M.D.E. Goodyear, M.B.,B.S.
E. Latimer, M.D.
M.E. McBride, M.D.
D. Nicholson, M.B., B.Ch.
C.L. Tanser, M.D.
J. Witcher, M.D.

Career Scientists:
G. Singh, Ph.D.

Chief Operating Officer:
I.B. Campbell, M.H.Sc.
(from Nov. 5/90)

Administrator:
C.E. Squires

Business Office Manager:
C.P. Freeman, R.I.A.

Senior Radiotherapy Technician:
B.J. Walker, R.T.
(to March 31/90)
B. du Bois, R.T.
(from Apr. 1/90)

Nurse Administrator:
G. Holmes-Brown, R.N.,B.A.S.
(to May 30/90)

Acting Nurse Administrator:
J. Scruton, B.Sc.N.
(from May 31/90)

Cancer Information Service:
B. Rigby, B.Sc.N., M.H.Sc.
(to Aug. 3/90)
T. McPhail
(from Aug. 4/90 acting co-ordinator)

Manager of Health Records:
D. Armstrong

Lakeview Lodge Supervisor:
C. Dawson, R.N.

On February 2, 1990, the Ministry of Health granted approval to begin construction of the new cancer centre building. By July, labor problems were resolved and construction progressed at a rapid pace. Before winter set in, all five stories had been erected and the building's exterior began to resemble the scale model provided by the architects Trevor Garwood Jones and Associates. Total construction and equipment costs are estimated to be $41,646,000 and expected occupancy is January 1992.

Since July, the influx of new patients extended waiting times up to 10 weeks for patients scheduled to receive radiotherapy. In part, this was due to several unforeseen circumstances: A sharp increase in the number of patients with complex problems (pediatric and Hodgkin's disease); a breakdown of one of our major linear accelerators (27 years old); and a shortage of radiation technologists. As a result, OCTRF reinstated a province-wide patient referral system. In August the referral centre was established in Hamilton to facilitate the access for Ontario residents to radiotherapy within a safe and reasonable period. Only those patients who were able and willing to travel and met the standards required for re-referral were treated at other regional cancer centres. Patients within our catchment area were referred to treatment at London, Thunder Bay, Toronto-Bayview and Windsor Regional Cancer Centres. By mid-November, patient waiting times fell to the normal length and the re-referral system was placed on reserve status. We are very grateful for the co-operation extended by our sister centres.

An overall increase in our patient load continued to strain facilities at the main Centre. In August, after a review of workload statistics, to provide additional clinic space, we relocated six radiation oncologists to offices on the third floor of Lakeview Lodge. A new system of communications has been instituted among many of the staff, All of whom are now located away from the main centre.

Enrollment has increased in the postgraduate residency training programs, with four trainees in radiation oncology and one in medical oncology. An illustrated brochure has been prepared describing the postgraduate oncology training program offered at McMaster and is being made available to all Canadian universities. The Department of Radiation Technology has stepped up recruitment and attracted students from as far away as Hong Kong, South Africa, England and Australia. In October, school of radiation was organized.

During the past year we welcomed several new staff members. On November 5, Ian Campbell, formerly of the Grey Bruce Health Centre, was appointed Chief Operating Officer. Ian brings to us a wealth of professional experience in health care administration. In May, Denise Lane was appointed project co-ordinator for the new Centre. She been employed by the London Regional Cancer Centre and Markham-Stouffville Hospital.

In April, Barb duBois became Senior Radiotherapy Technologist following the retirement of Bev Walker after 35 years' service. Joanne Dufay has joined the Department as assistant manager.

June Scruton became Acting Nurse Administrator on May 31, following the departure of Gayle Holmes-Brown, who accepted a position as Assistant Director of Nursing at our host hospital. Brenda Johnstone joined the nursing department as nurse administrator for education and research.

In August, Teresa McPhail became Acting Co-ordinator of Cancer Information Services, taking over from Barb Rigby, who left to pursue further challenges.

On August 15, Dr. Peter McCulloch resigned as Head of Medical Oncology and took a three-month study leave. Dr. Mark Levine, Head of Clinical Trials, has assumed the post of Acting Head until a selection committee finds a permanent replacement for Dr. McCulloch.

In December, the Centre said farewell to Dr. Alfy Tadros, senior radiation oncologist, who, after 23 years at the Hamilton Regional Cancer Centre, leaves to take up duties at the Cancer Treatment and Research

Foundation of Nova Scotia in Halifax. Drs. Malti Patel and Gordon Okawara accepted full-time positions in the Department of Radiation Oncology, after completing their residency training in Hamilton.

Academic and clinical research activities continue to focus on improving methods of cancer treatment and on developing supportive cancer care programs. In April, the 1990 New Horizons Committee announced their first lecture series "Enhancing Wellness: Trends and Issues for the '90s". This Committee focuses on oncology nurse education, in particular new trends developing in cancer nursing. Regional oncology rounds hosted eight visiting speakers during the 1989-90 academic year, with the support of Adria Laboratories of Canada Ltd. The monthly clinical trials dinner meetings, which continue are a constant source of valuable information and a means of medical audit.

On October 11-12, Dr. Jim Gowing, co-ordinator for Outreach for Central-West Region, attended the National Conference on Community Cancer Care in Winnipeg. He was the OCTRF representative on the program planning committee. This two-day conference was attended by representatives of all provincial governments, Ministry of Health, Health and Welfare Canada, and Canada 2000. The conference addressed the development of strategic alliances, challenges and action guidelines for community-based, cancer-care programs.

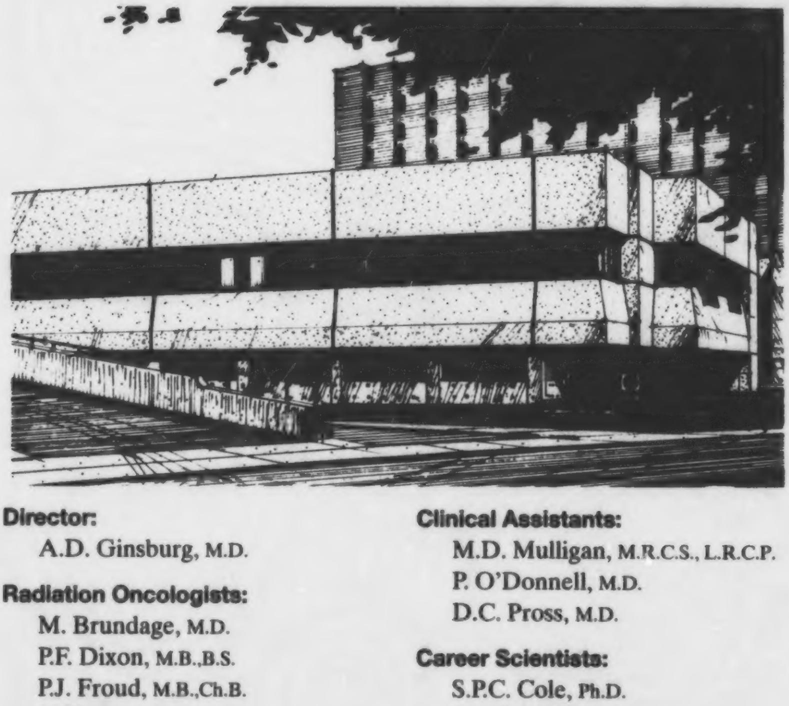
The Canadian Cancer Society, through a generous donation, provides music therapy for our patients in the treatment and chemotherapy departments of the HRCC and the Henderson Hospital.

In order to foster excellence in patient care, teaching and research programs, the Centre's senior management staff has begun a process of organizational restructuring to better effect long-term planning and resource management in the new Centre. These changes include the development of a Senior Management Advisory Committee, Medical Staff Advisory Committee, and several standing committees which report to both these groups on a monthly basis. These committees provide a forum, involving staff in strategic planning and decision-making that will enhance the performance of a comprehensive cancer centre.

Heather M. Hiscox
Administration

KINGSTON REGIONAL CANCER CENTRE

KINGSTON GENERAL HOSPITAL



Director:

A.D. Ginsburg, M.D.

Radiation Oncologists:

M. Brundage, M.D.
P.F. Dixon, M.B.,B.S.
P.J. Froud, M.B.,Ch.B.
V. Kraus, M.D.
N.J. Mackillop, M.B.,Ch.B.

Medical Oncologists:

B.J. Campling, M.D.
E.A. Eisenhauer, M.D.
P.R. Galbraith, M.D.
W.S. Lofters, M.D.
J.L. Pater, M.D.

Clinical Assistants:

M.D. Mulligan, M.R.C.S., L.R.C.P.
P. O'Donnell, M.D.
D.C. Pross, M.D.

Career Scientists:

S.P.C. Cole, Ph.D.
J.S. Gerlach, Ph.D.
J.C. Kennedy, M.D.

Physicists:

J. Robins, M.A.
P.C. Shragge, Ph.D.
J. Szabo

Honorary Medical Consultant:

R.C. Burr, M.D.

Administrator:
J. Perrin, D.H.A.

Head Nurse:
S. Fenwick, Reg.N.

Chief Technician:
N. Hobbs

Social Worker:
D. Forster, M.S.W.

Manager of Health Records:
R. MacDonald, C.C.H.R.A.(C)

Quinte-Thousand Island Lodge Supervisor:
D. Broeders, Reg.N.

In June 1989 the Kingston Regional Cancer Centre, responding to provincial concerns about shortage of treatment facilities, offered to expand its services to provide care to oncology patients from an additional five counties—Durham, Victoria, Peterborough, Northumberland and Haliburton. We have started an outreach clinic in Peterborough and are developing contacts with the Peterborough and area physicians, recognizing how difficult it must be to change traditional referral patterns.

In the 15 months since accepting this new responsibility, 324 patients have been referred from the new catchment area. When the period July 1988 to June 1989 is compared with the period July 1989 to June 1990, we see an increase of 20% in the number of patients receiving radiation.

Currently the waiting time for radiation treatment is virtually zero—a tribute to the dedication of the staff of the Centre at many levels, the management skills of Mrs. Nancy Hobbs, manager of radiation technology, and the support of the Ministry and the OCTRF in recruiting technologists and in funding the expanded program. However, the increase imposed some considerable stress because it preceded and, indeed, still precedes the hiring of adequate staff. Also there is now considerable pressure on space and equipment.

The Kingston General Hospital, as so often before, rallied around us and is providing interim space and is planning medium-term rearrangements with us. With consultants from Ernst and Young, we are developing a 10-year strategic plan which will take into account a projected doubling or even tripling of patient referrals over this time; the need for equipment; an increasing requirement for expanded space; and staffing projections.

Key staff appointments: Bill Mackillop has returned to our Centre as head of radiation oncology, Joyce Perrin joined us as centre administrator; Shauna Fenwick as director of nursing; Bill McAllister as head of computing; Donna Forster as our social worker; and Donna Dechant as human resources officer. The radiation technology staff has expanded significantly, and the health records room staff is growing.

A new dictaphone system greatly facilitates patient charting and we await the new OPIS computing system with much anticipation and some trepidation. As physicians we have begun to exploit the power of computers and have developed a number of prospective data bases and have produced some outcome studies in a number of disease sites.

A patient satisfaction survey, done some time ago, suggests that our services are well-received. It suggested some changes and these will be implemented in the coming year. The nursing role has been greatly enhanced and we have undertaken a number of psychosocial initiatives, which are described elsewhere in this issue.

This year, we have advanced multidisciplinary patient care, one of our major goals, by establishing a colorectal oncology clinic, a skin cancer clinic, and by the imminent establishment of conjoint uro-oncology clinics.

Under the auspices of Nancy Hobbs and Siobhan McArdle and with the strong support of our radiation oncologists and physicists we launched a fully-accredited training program in radiation technology. Our first two candidates—Joanne Barclay and Gail Blasco—graduated in 1990.

Through the formation of a "critical mass" of researchers in Botterell Hall and under the leadership of Roger Deeley, research in basic sciences continues to flourish. Jim Kennedy and the Royal Military College group have maintained their momentum in phototherapy research. Bill Mackillop and Carol Quirt have continued their research in psychosocial oncology, and the radiation oncologists have made plans for applied research in their field. Through the auspices of Cliffe Lofters, the Centre's participation in clinical trials has increased enormously, and we continue to bask in the reflected glory of the NCIC Clinical Trials Group which is based in Kingston.

A.D. Ginsburg, M.D., FRCPC
Chief Executive Officer

LONDON REGIONAL CANCER CENTRE

VICTORIA HOSPITAL

London Regional Cancer Center

Chief Executive Officer:

L. Levin, M.D.

Radiation Oncologists:

C.T. Ago, M.B.,Ch.B.
A.Cooke, M.D.
A.R. Dar, M.B.,B.S.
B. Fisher, M.D.
L.E. Gaspar, M.D.
J.A. Gilchrist, M.B.,B.S.
J.A. Hammond, M.D.
A.L. Houghton, M.B.,Ch.B.
F. Perera, M.D.
A.T. Porter, M.D.
V. Venkatesan, M.B.,B.S.

Medical Oncologists:

V. Bramwell, M.B.,B.S.
G. Cairncross, M.D.
W.I. Kocha, M.D.
R.C. Lohmann, M.D.
D. Macdonald, M.D.
W. Mertens, M.D.
J. Skillings, M.D.
M.A. Taylor, M.D.
K. Tonkin, M.D.
T.A. Vanderberg, M.D.

Physicists:
A. Akinradewo, Ph.D.
R. Barnett, Ph.D.
J. Battista, Ph.D.
D.J. Dawson, Ph.D.
P. Munro, Ph.D.
E. Papiez, Ph.D.
L. Papiez, Ph.D.
J. Schroeder, M.Sc.

Scientists:
Career:
A. Chambers, Ph.D.
J. Harris, Ph.D.
W.R. Inch, Ph.D.
D.J. Koropatnick, Ph.D.
Other:
G. Hammond, Ph.D.
R. Khokha, Ph.D.

Chief Operating Officer:
B. Paulse, M.H.A.

Director, Financial Services:
B. Hodgert, C.G.A.

Director, Health Information Services:
D.G.E. Ross, C.C.H.R.A.
Administrator, London Breast Screening Clinic:
J. van der Holt

Medical Co-ordinators:
L. McCurdy, M.D.
K. Sparrow, M.D.

Director, Nursing Services:
E. Anderson, M.Sc.N.

Nutrition Manager:
D. Goettler, M.Sc.

Director, Community Cancer Outreach Program:
S. Markland

Director, Radiation Therapy Technology:
P. deSilva, R.T.T.

Social Work Manager:
A. Sawarna, M.S.W.

Director, Thameswood Lodge:
C. Sellery, B.Sc.N.

During the past year, the London Regional Cancer Centre has concentrated on building a sound infrastructure through an extensive quality assurance program as we move towards formal accreditation at the beginning of 1991. Furthermore, during the past year, through collaborative interaction with department head, this Centre has produced a strategic plan that sets priorities at all levels.

During the past year, the Centre's continued emphasis on a strong radiotherapy program was further enhanced through full membership in the Radiation Therapy Oncology Group, continued international leadership in developing a portal imaging system, and sustained leadership in the use of unsealed radioactive sources such as Strontium-89, and novel, sealed radioactive sources such as Ytterbium in brachytherapy. In recognition of the serious shortage of Canadian-trained radiation oncologists, the Division of Radiation Oncology has substantially increased its residency training program for 1991. Despite significant shortages in radiation therapy technologists (RTTs), the London Regional Cancer Centre continued to provide radiotherapy to the people of southwestern Ontario. We have recruited additional RTTs through the OCTRF recruitment drive and, in 1991, hope to train more RTTs through an expanded program.

In medical oncology, the NCIC-sponsored, three-year interleukin-2 study into the treatment of melanoma and renal-cell carcinoma will complete accrual this year. We will continue our studies into the use of other biological response modifiers. The Centre will maintain its commitment to an autologous, bone-marrow-reinfusion program and will continue to facilitate allogeneic bone-marrow transplantation.

In July 1990, we opened the first Breast Screening Unit in Ontario. In November, Hon. Marion Boyd, Minister of Education, and MPP for London Centre, conducted the official opening ceremony. This new undertaking in the area of early cancer detection will screen 13,000 women per year in London. It is envisaged that a second unit will open in this region in 1991. These pioneering initiatives reflect the dedication of the Southwestern Ontario breast Screening Program administrator, Joan van der Holt and the medical and radiology co-ordinators, Drs. Lauren McCurdy and Keith Sparrow.

The Community Cancer Outreach Program (CCOP) continues to provide strong linkages with the community. During the past year, this program opened a library in the Centre to provide information to patients and their families. We held numerous workshops for health-care professionals in the regional and the program presented a second successful public lecture series in the Centre and gave talks during visits to schools and service groups. We held a second, fully subscribed, successful "Evening Out" for women who have cancer, emphasizing nutrition, exercise, skin care and comfortable clothing. *ONCORE,* the London Regional Cancer Centre's journal aimed at health-care professionals, continues to be well received nationally with a quarterly distribution of 10,000 copies.

The cancer research laboratories provide an excellent opportunity for interface research with medical and radiation oncologists. It is gratifying to report that peer review grant support for this program has been increasing steadily over the last three years.

During the past year, we welcomed Drs. Andrew Cooke, Tetteh Ago, Varugar Venkatesan and Jim Gilchrist as staff radiation oncologists and Drs. Katia Tonkin and Marianne Taylor as staff medical oncologists. We also welcomed Dr. Peter Munro and Drs. Lech and Ewa Papiez as staff physicists and Dr. Rama Khokha as a scientist funded through regionally designated funds and Victoria Hospital.

During the past year, Dr. Arthur Porter, Chief of Radiation Oncology, was invited to the University of London (U.K.) as a visiting professor. He also delivered the Sterling Lecture at the Advanced Oncology Symposium of the Royal College of Physicians. Dr. Porter, one of two Ontario physicians on Cancer 2000, a national group targeting the projected needs of cancer patients in the year 2000, has been appointed Chairman of the OCTRF Professional Advisory Committee on Radiation Oncology. In London in December, Dr. Vivien Bramwell, Chief of Medical Oncology, chaired a Terry Fox Workshop entitled The Molecular Biology of Sarcoma. Dr. Jerry Battista, Chief Physicist, was invited to Australia and New Zealand by the Australian College of Physical Scientists and Engineers in Medicine, in October. He delivered seven lectures in six cities. Dr. Battista has been elected Chairman of the OCTRF Professional Advisory Committee on Medical Physics. Dr. Greg Cairncross, a neuro-oncologist, was invited to lecture at Erasmus University, Rotterdam and the University of Leiden, Leiden, the Netherlands. His topic was supratentorial anaplastic glioma in adults. In April in Miami, Florida, he also chaired the neuro-oncology scientific session at the American Academy of Neurology meeting. Dr. Laurie Gaspar, radiation oncologist, lectured in San Diego, California on the use of brachytherapy in esophageal cancer. Dr. Jamey Skillings, medical oncologist and Medical Director of Biometrics, was appointed the provincial chairperson of the colorectal disease site team. Dr. Ted Vandenberg was awarded a grant from the Maude Katherine Taylor Cancer Research Fund.

In April, Dr. Ann Chambers, career scientist, presented a seminar at Waksman Institute of Microbiology at Rutgers University, New Jersey. Also she was invited to speak and participate in a workshop on SPP1 phosphoprotein held by the Texas Mineralized Tissue Society in Kerrville, Texas in May. Dr. Chambers made a presentation to the special invited session of the Third International Congress of the Metastasis Research Society, in Bethesda, Maryland in September. She was an invited speaker at the annual meeting of the American Society for Therapeutic Radiology and Oncology (ASTRO) in Miami, Florida in October. Radiation oncologists from the London Centre presented nine papers at the annual meeting of the Canadian Association of Radiation Oncologists (CARO) held in September. Dr. Jay Engel, a fellow in radiation oncology in London, won second prize for papers presented by residents at the CARO meeting.

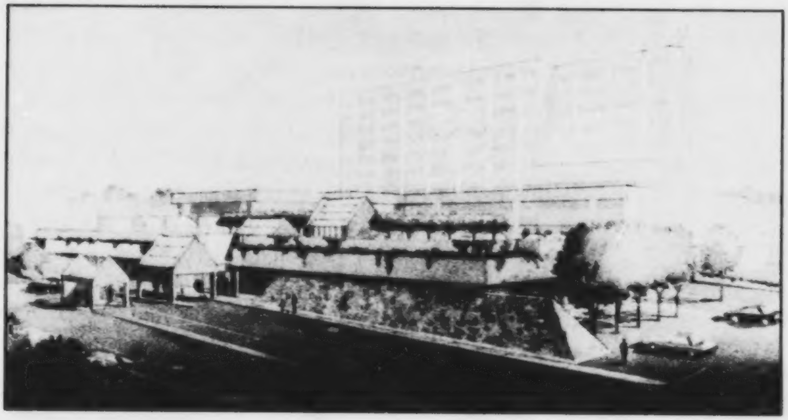
Shelley Markland, Director of CCOP, spoke at the National Conference on Community Cancer Programs in Winnipeg in October. Dianne Goettler, Manager of Nutrition, received the 1990 Peer Recognition Award from the Ontario Dietetic Association. Rosemary Allaster, Primary Nurse in Neuro-oncology, was selected to participate in a Rotary Group Study Exchange with Australia. During her six weeks in New South Wales, Rosemary made 26 presentations. On her return to Canada, Rosemary was named the Paul Harris Fellow, the highest recognition granted by Rotary International. Veda Goodwin, social work, was notified that her videotape "Doug and Darlene" was accepted for the film screening competition at the 8th International Congress on Care of the Terminally Ill in August.

In the spring, Dr. Leslie Levin spoke about ovarian cancer at closed international meeting held in Graz, Austria. He also made a presentation to the second meeting of the International Gynecologic Cancer Society in Toronto in the Fall and lectured about the importance of dose intensity at the Royal College of Obstetricians and Gynaecologists in London, England.

L. Levin, M.D.
Chief Executive Officer

NORTHEASTERN ONTARIO REGIONAL CANCER CENTRE

LAURENTIAN HOSPITAL, SUDBURY



Chief Executive Officer:
R.E.T. Corringham, M.B.,B.S.

Radiation Oncologists:
R.J. Bissett, M.D.
P.D. Lefebvre, M.D.

Medical Oncologists:
P.O. Cano, M.D.
C.J. Germond, M.B.,Ch.B.
C.L. Sinoff, M.B., B.Ch.

Clinical Fellow:
C. Toze, M.D.

Clinical Assistants:
G.M. Kane, M.B., B.Ch.
H.D. McConnell, M.D.

Physicists:
P. Dunscombe, Ph.D.
P. McGhee, Ph.D.
T. Chu, M.Sc.

Psychologist:
S. Steggles, Ph.D.

Epidemiologist:
V. Nguyen, Ph.D.

Research:
A.D. Ho, M.D., Director
M. Lu, Ph.D.

Chief Operating Officer:
B.L. Valin, M.B.A.

Manager, Financial Services:
M. Poirier, C.G.A.

Manager, Patient Care Services:
C. McChesney, B.Sc.N.

Chief Technologist, Radiation Therapy:
J. Palmer, R.T.T.

Nutritionist:
S. Lamoreaux, R.P.Dt.

Manager, Health Information Services:
R. Zambelli, C.C.H.R.A.(C)

Manager, Computer Services:
G. Roy, B.Sc.

Librarian:
E. Ho-Tsui, M.A.

On November 5, 1990, the Northeastern Ontario Regional Cancer Centre (NEORCC) began operations when its first patient received radiation. While the staff have been preoccupied with their efforts to bring the new Centre "on stream", we have provided consultation and chemotherapy to patients for more than six years from temporary quarters in Laurentian Hospital. In the first nine months of 1990, 800 new patients were seen and it is projected that we will see 1500 patients in our first year of operation.

Staffing changes and additions have dominated preparations for the Centre's opening. We welcome Drs. Colin Germond and Pablo Cano as medical oncologists, Dr. Cynthia Toze as clinical fellow and Dr. Dianne McConnell as clinical assistant. Dr. Germond was named interim head of medical oncology following the departure of Dr. Glen Goss for Ottawa. Dr. Cano will develop our continuing care program. This year we lost Dr. Mark Vincent who moved to Ottawa as senior resident to complete Royal College Fellowship requirements. Dr. Pierre Lefebvre has joined Dr. Randy Bissett as staff radiation oncologist. Dr. Bissett is interim head of radiation oncology. Dr. Barbara Lada of Ottawa also has joined this department. Dr. Peter Dunscombe is our new head of medical physics and Jane Palmer heads up our radiation technology team.

The NEORCC has absorbed the Sudbury peripheral cancer clinic which the Princess Margaret Hospital has operated for the past 25 years. In September 1990, the NEORCC also took over the North Bay peripheral clinic. Now the NEORCC will meet most of the demand for radiation therapy in the North and will reduce the waiting time for such treatment throughout the Province.

In April 1990, Dr. Anthony Ho, a hematologist-oncologist previously at the University of Heidelberg, joined the Centre as director of research. With co-workers, including Dr. Ming Lu from the Banting Institute in Toronto, the team will pursue research in the following areas: The use of peripheral stem cells for transplantation; new strategies in purging bone marrow; and the immunologic effects of hematopoietic growth factors. Dr.

Ming Lu has special interest in studying the development of leukemia and lymphoma at the gene level.

In the area of clinical trials, we are developing a transplantation program for patients with solid tumors using stem cells from the peripheral blood. Other clinical trials using hematopoietic growth factors are being developed with the co-operation of pharmaceutical companies that specialize in biotechnology. A successful multicentre trial in small cell lung cancer has been conducted in co-operation with other Northern Ontario Centres.

We now have a formal affiliation with the University of Ottawa and have embarked on a number of collaborative initiatives including cross appointment of professional staff to the Faculty of Medicine and co-operation in the development of training programs for radiotherapy technicians and physicians.

Staff have increased to 100 and we project 120 employees by April 1991. An active world-wide recruiting program has given us an international staff from Canada, Europe, Africa, Australia and Asia.

Shortages of radiation and medical oncologists, radiotherapy technicians and other key professional groups continue to be a source of deep concern. Nonetheless, the year is marked with a sense of accomplishment because the NEORCC now is able to assume its full role in providing cancer treatment and research to the people of the Northeast. We thank staff and community and our OCTRF family for their support and will work to ensure optimal cancer care networks necessary in Northeastern communities.

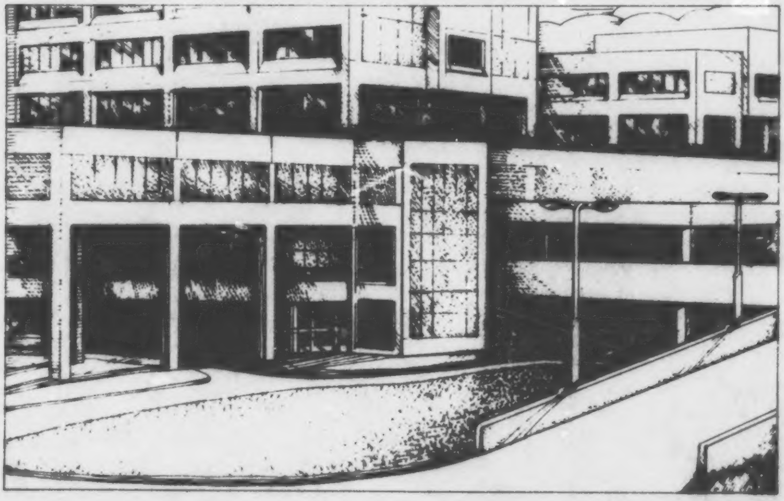
R.E.T. Corringham, M.B.,B.S.
Chief Executive Officer

OCF

OTTAWA REGIONAL CANCER CENTRE

OTTAWA CIVIC HOSPITAL

AND OTTAWA GENERAL HOSPITAL



Chief Executive Officer:
W.K. Evans, M.D.

Radiation Oncologists:
J. Crook, M.D.
C.J.E. Danjoux, M.D.
Division Head
L. Eapen, M.D.
B. Esche, M.D.
P. Genest, M.D.
A.L. Girard, M.D.
L. Grimard, M.D.
C. Lochrin, M.D.
B.D. Nair, M.B.,B.S.

Medical Oncologists:
S. Aitken, M.D.
C. Cripps, M.D.
R. Goel, M.D.
G. Goss, M.D.
D. Logan, M.D.
J.A. Maroun, M.D.
Division Head
D.J. Perrault, M.D.
D.J. Stewart, M.D.
S. Verma, M.D.
V.P.J. Young, M.D.

Clinical Assistants:
H. Bastianelli, M.D.
T. Capruciu, M.D.
M. Carew, M.D.
J. Chouinard, M.D.
P. Craigie, M.D.
G. Knight, M.D.
S. Langlois, M.D.
K. O'Toole, M.D.
I.A. Prosser, M.D.
M. Reed, M.D.
K. Robillard, M.D.
M. Touchie, M.D.
S. Wong, M.D.

Career Scientists:
H.C. Birnboim, M.D.
R.G. Liteplo, Ph.D.
R. Hawley, Ph.D.

Physicists:
I. Cameron, Ph.D.
J. Cygler, Ph.D.
L.H. Gerig, Ph.D.
G.P. Raaphorst, Ph.D.
Division Head
D. Salhani, Ph.D.
M. Soubra, M.Sc.
J. Szanto, M.Sc.

Chief Operating Officer:
E. Wall, D.H.A.

Financial Services Manager:
E. O'Reilly, CMA

Human Resources Administrator:
D-L. Menard, B.A.

Executive Secretary:
D. Pineau, C.M.S.

Nurse Administrator:
B. Skinn, M.Sc.N.

Nurse Managers:
J. Catton, B.Sc.N.
(Civic Hospital Division)
L. Fawcett, B.Sc.N.
(General Hospital Division)

Head, Radiation Technology:
R.P. Wallace, A.C.(T)

Managers of Health Records:
S.A. Parsons, C.C.H.R.A.(C)
(Civic Hospital Division)
M. Brassard
(General Hospital Division)

Manager, Computer Services:
T. Wadsworth, B.Admin.

Lodge Manager:
I. Martin, R.N.

The Ottawa Regional Cancer Centre (ORCC) has come through a tumultuous year and many changes. The Centre's principal objectives this year were to refine further the organizational structure and to meet some of our human resource and capital needs. During the year, Dr. Cyril Danjoux became our Head of Radiation Oncology. He brings to his new position well recognized talents in clinical research, administration and teaching. His first appointment to the Division of Radiation Oncology is Dr. Catherine Lochrin who trained at the ORCC and recently returned from postgraduate training with Prof. S. Dishe at the Mount Vernon Hospital in Northwood, Middlesex, U.K. During her fellowship year, Dr. Lochrin's research focussed on the application of continuous hyperfractionated accelerated radiotherapy to the treatment of advanced tumors of the head and neck, bronchus and esophagus and the investigation of human tumor-cell kinetics using *in vivo* Budr techniques. Dr. Danjoux is searching for more academically oriented radiation oncologists to meet the current shortage at the ORCC. Dr. Jean Maroun, Head of Medical Oncology, has appointed Drs. Rakesh Goel to the Civic Division and Glenwood Goss to the General Division. Dr. Goel trained in medical oncology at the W.W. Cross Cancer Institute in Edmonton, Alberta and did postgraduate studies in clinical pharmacology in San Diego, California. Dr. Goss has been recruited to direct the lung cancer program at the ORCC. He will strengthen the clinical research program and enhance the interaction between clinicians and basic researchers who wish to investigate the cellular and molecular biology of lung cancer.

Dr. Danielle Perrault is now the medical co-ordinator for the Breast Screening Program in the Ottawa region. She has recruited Ms. Suzie Joanisse to be her administrative co-ordinator and has assembled a coalition representing professional groups from the six area hospitals, representation from the District Health Council, and the Canadian Cancer Society as well as women from the community. This group is working together to identify strategies to implement breast screening, in a fashion that will achieve the goal of screening 70% of the women in the target population, ages 50 to 69 years.

We welcome Ms. Esta Wall, as the Centre's Chief Operating Officer. She has had previous experience in directing health-care facilities in Toronto and has worked within the Ministry of Health. Since her arrival on August 13, 1990, she has resolved a number of outstanding issues and it is evident that the Centre will benefit greatly from her administrative skills. Mrs. Hilda Ginsburg, who is the Centre's new Purchasing Officer, will supervise the newly established centralized purchasing system; this system promises to achieve substantial savings as the purchasing officer negotiates the best possible prices for the Centre's capital equipment and supplies. Ms. Debra-Lynn Menard, our new Human Resources Administrator, will ensure that the Corporate Human Resources policies are implemented in the ORCC and will deal with the many human resource issues that arise among a large staff.

This past year an operational review of the nursing services of the ORCC made several recommendations aimed at optimizing the nursing department's organizational structure and function. Ms. Barbara Skinn, Nurse Administrator, and her nurse managers have worked hard to restructure the department, recruiting staff to provide quality patient care and developing a nursing documentation system. Ms. Jane Catton, the new Nurse Manager at the Civic Division, brings invaluable knowledge, experience and leadership skills to this challenging position. Both Divisions of the ORCC have a nurse manager on site who is responsible for the daily management of the nursing services. A clinical teacher-nursing educator has been recruited to augment the nursing staff's clinical expertise. In addition, a social worker with experience in women's health and sexuality issues has joined the psychosocial team. These changes promise to enhance our nursing practice and improve the quality of care provided at the ORCC.

Ms. Johanna Stapleton, staff nurse, is now Special Projects Nurse for the ORCC. In this term position, Johanna completed the Nursing Policy and Procedure Manual.

Mrs. Louise Fawcett, Nurse Manager at the General Division, has fulfilled all requirements for her B.Sc.N. degree. Ms. Barbara Skinn, R.N., B.Sc.N., M.Sc.N., now holds a cross appointment as clinical assistant at the University of Ottawa. In this collaboration, Barbara hopes to develop the research and educational components of the ORCC's nursing program.

Members of the Nursing Department have been working with those of Health Records to develop and implement a nursing documentation system which accurately and consistently records the patient care provided by the staff. The recommended documentation system is CBE (charting by exception)—a process which is based on a nursing history, flow sheets, progress notes and standard care plans. This system allows the nursing staff to record their patient-care activities while it provides a mechanism to monitor workload and communicate the nurses' roles and functions to other members of the patient-care team.

In October 1990, Ms. Debbie Gravelle, Charge Nurse, General Division and Barbara Skinn, Nurse Administrator, attended the Cancer 2000 Conference in Winnipeg to discuss and explore the issues surrounding the development of community cancer control networks. They presented their experiences in managing the Centre's peripheral clinics and at the same time gained useful information that will help the Centre to extend its own outreach.

During 1989, the Department of Radiation Technology had a substantial increase in patient load, even though there was a shortage of radiation technologists. The department treated an additional 117 patients from the Toronto and Sudbury areas during the fall of 1989, when the Princess Margaret Hospital had to restrict its intake of new patients. The ORCC was able to accommodate these additional patients largely because of the dedication and extra effort of its radiation technologists.

Lynda Jackson, Louise Fitzmaurice and Catherine Waugh, graduates of the radiation technologist training program, received certification diplomas from the Canadian Association of Medical Radiation Technologists. Lynda Jackson also won the Association's award for the best student essay and Ruby Lafleur won the Ottawa Section's essay competition.

In February 1989, the first ORCC patient was treated with our new Siemens KD-2 linear accelertor after the Hon. Elinor Caplan, the then Minister of Health of Ontario, presented it to the Centre.

Mr. Ron Wallace, Head of Radiation Technology, is chairman of the 50th Anniversary Conference of the Canadian Association of Medical Radiation Technologists, which will be held in Ottawa in 1992.

During the past year, Mrs. June Davidson stepped down as the manager of Maurice J. Grimes Lodge. Now Ms. Irene Martin, of Alta Vista Lodge, is manager for both of the Centre's Lodges. In this expanded role, Irene will ensure a high quality of service and comparable programs in both lodges. Last year, Irene established the first "Humor Room" ever provided in a cancer lodge. This Humor Room at the Alta Vista Lodge has been named "the Laugh-Inn" or "La Rigolade" and soon a second Humor Room will be opened in the Maruice Grimes Lodge. Each will contain a variety of humorous books, audiocassettes and videocassettes in the hope that the lodge residents will discover that "laughter is the best medicine".

Dr. Janos Szanto, who graduated from the medical physics training program, is a new medical physicist at the ORCC. Dr. Alex Kania joined the Medical Physics Department as a medical physics trainee and Drs. Sanjiv Samant and Tewfik Bichay joined as research fellows. These new staff members will assist the further development of the Centre's clinical Physics and Radiotherapy Departments and will strengthen various aspects of our research program.

During the past year, Siemens Electric Limited awarded a research contract to the ORCC to further develop and model computer-controlled radiotherapy and characterize radiation output of the KD-2 linear accelerator.

The ORCC has formed the Medical Physics Organized Research Unit (MPORU) in collaboration with our physicists, Carleton University, the National Research Council and other institutions. Dr. Peter Raaphorst is MPORU's first chairperson. We now offer a full slate of graduate courses in medical physics for M.Sc. and Ph.D. physicists. At present, this program has 13 graduate students and its graduate, Bruce Faddegon, has completed his Ph.D.

Working together, Drs. Raaphorst, Stewart and Danjoux are developing focussed research on mechanisms of resistance to cancer therapy. This focussed approach has resulted in several collaborative research projects. The development of this working group has been facilitated by the approval of a new career scientist position. Dr. Chang Ng, a research biophysicist from Johns Hopkins University, will join our research staff in the new year.

At present, the Centre's Department of Experimental Oncology has three career scientists—Drs. H.C. Birnboim, R.G. Hawley and R.G. Liteplo. All conduct their research under grants from the National Cancer Institute of Canada; Dr. Birnboim also has a grant from the Medical Research Council of Canada. In addition, Dr. Hawley has a grant from the Arthritis Society of Canada and one from the Leukemia Research Fund.

In April 1990, the ORCC presented the 12th Cancer Research Conference entitled The Molecular Biology of Cancer. The organizing committee consisted of Drs. Chaim Birnboim, Peter Raaphorst, Cyril Danjoux and W.K. Evans working under the chairmanship of Dr. Diane Logan. Dr. R.G. Hawley opened the meeting with an "overview" of the subject. Other papers included one on the role of transgenic mice, the *neu*-oncogene in breast cancer, anti-oncogenes and the clinical exploitation of oncogenes, and chromosomal translocations in malignant lymphoma. One session, which discussed molecular mechanisms of tumor-cell resistance, included talks on metallothionein and the DNA basis of radiation sensitivity. The keynote speaker was Dr. I.B. Einstein, Director, Comprehensive Cancer Society, Columbia University, New York.

After the conference, the Department of Experimental Oncology organized a mini-course for clinicians, which gave about a dozen of our Centre's clinicians "hands-on" experience with some of the new techniques in molecular biology. The instructors for this mini-course were graduate students working in the Department of Experimental Oncology and with the University of Ottawa Cancer Research Group. Both the clinicians and the graduate students declared that this mini-course was a great success.

Preparations for the expansion of the research facility at the General Division are proceeding well. The research floor will house both the Department of Experimental Oncology's laboratories and members of the University of Ottawa's Cancer Research Group (Drs. M. McBurney, J. Bell and D. Gray) and the Centre's clinician scientists, Dr. D. Logan. Once it is established in its new facility, this research group will provide a focus for research in cell and tumor biology in Ottawa.

The success of the present research programs has strained to the limited existing laboratory space. Until the new research floor is completed, Dr. Hawley will work in space provided by the medical school. Although this new arrangement has created some inconvenience, it will allow some expansion of research over the next few years while the new research floor is being built. During the past year, Dr. Hawley served as a member of the National Cancer Institute of Canada's molecular biology grant panel and Dr. Birnboim served on the genetic panel of the Medical Research Council of Canada as well as the Cancer Research Society's grants panel.

The Department's activities had an international flavor this year. Two scientists from Brazil spent the year with us and after their return home, Dr. Birnboim was invited to Brazil to speak to the PanAmerican Association of Biochemical Societies.

During the past year, the Centre has dealt with increasing numbers of patients with inadequate numbers of staff and with increasing technical problems related to aging equipment at the Civic Division. Frequently there have been long waiting times for treatment but, at the time of writing, these have eased somewhat because we have recruited additional radiation technologists and have operated over extended hours. Unfortunately, at the Civic Division, productivity was compromised because of the frequent breakdown of the Division's two linear accelerators. Both are now 12 years old and, over the last year, the Therac-6 has had an average "downtime" of one day per week. In addition, the Therac-20 is "down", on average, one half-day per week. At the same time, the Division's lone simulator is in need of replacement. Because of waiting lists, we could not introduce a simple sequential replacement strategy at the Centre and have proposed an alternative strategy, namely, the creation of a new dual simulation suite and conversion of the old simulator bunker to a linear accelerator bunker. We hope that this project soon will be approved by the Ministry of Health and that they will allow us to upgrade the Civic Division's radiotherapy equipment while preparing for additional machine capacity at the Centre.

The Centre is also planning to expand its facilities at the General Division. On October 31, 1989, the Hon. Elinor Caplan, the then Minister of Health, announced that the Centre would undergo a major expansion. With the assistance of the architectural firm of Bregman & Hamann, we are developing plans for this 27-million dollar project. All hope that the expanded facility will open in mid-1993.

W.K. Evans, M.D., FRCPC
Chief Executive Officer

OCF

THUNDER BAY REGIONAL CANCER CENTRE

GENERAL HOSPITAL OF PORT ARTHUR

ONTARIO CANCER TREATMENT
AND RESEARCH FOUNDATION

Chief Executive Officer:
J.F. Kotalik, M.D.

Radiation Oncologists:
S. Gulavita, M.B.,B.S.
M. McLean, M.B., B.Ch.

Medical Oncologist:
H.S. Dhaliwal, M.D.
H.L. Rayner, M.D.

Clinical Assistant:
L. Pratt, M.D.

Physicists:
M. Al-Ghazi, Ph.D.
B. Arjune, M.Sc.

Psychology Department:
S. Sellick, Ph.D.
H. Neilson, B.S.W.

Chief Operating Officer:
M. Civitella, M.H.S.A.

Financial Services Manager:
M.M. Ryan

Nurse Administrator:
L. Bright, Reg.N.

Radiation Therapy Manager:
J.V. Morgan, R.T.

Clinical Trials Manager:
E. Rayner, R.N.

Health Information Services Manager:
M. Kelly, C.C.H.R.A.(C)

Amethyst Lodge Supervisor:
M. Magnusson

This year, the Thunder Bay Regional Cancer Centre (TBRCC) made significant progress towards the development of a comprehensive oncology program for Northwestern Ontario.

Over the past three years, we are providing more comprehensive care following the addition of two full-time medical oncologists, an administrator, a psychologist, a social worker, a clinical trials nurse and manager, a junior physicist, a physics assistant and a radiation therapy clinical instructor. With the perception of better care, regional physicians have increased their referrals and thus increased our workload. Now residents of Northwestern Ontario are more likely to seek cancer care in Thunder Bay rather than Southern Ontario, Manitoba or the United States.

The Centre now provides the full range of multidisciplinary oncology care, research and education which serves as the basis for cancer programs including personal contacts in the community. The Community Cancer Care Network is an essential component in the delivery of cancer services in Northwestern Ontario. This year the addition of Atikokan has increased to seven the number of outreach clinics. While this activity permits decentralization of services, we must now ensure that this effort does not compromise service delivery and treatment outcomes.

To meet these challenges, we are working toward an effective infrastructure, which will support the delivery of service to a large area of Northwestern Ontario. We have established new structures and committees to handle more effectively internal and external policies and operations.

For several years now, operation of the Centre has been hampered by a critical shortage of space. This year the TBRCC is at a delicate stage in its development; from this point onwards, we can maintain and enhance existing programs only if we are supported with adequate outpatient and inpatient facilities. As in all other centres, we can offer the citizens of Northwestern Ontario new initiatives in prevention and treatment of malignant diseases.

Because we need adequate facilities to attract and maintain specialists to this region, it became imperative for TBRCC to re-evaluate its short and long-term development plans; in this effort, we will work closely with our host institution, the Port Arthur General Hospital, to develop a comprehensive cancer program for Northwestern Ontario.

Although our staff has devoted much time to the development of the functional plan, we have completed several patient-focused projects. The Centre has committed itself to seek accreditation hence we are in the process of developing a quality-assurance program. Also the Centre has developed a new patient information brochure, a sympathy card, a chemotherapy video for patient education, and is close to distributing its first community newsletter.

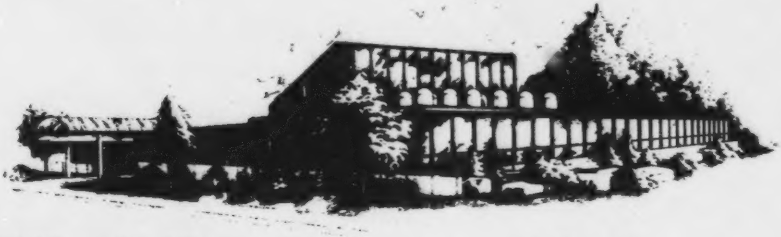
We are confident that we will meet the challenges facing us in the new year. We are optimistic because we have a dedicated staff who wants to be part of a strong and growing organization and whose ultimate goal is the delivery of quality patient care, teaching and research programs.

J.F. Kotalik, M.D., D.M.R.T., FRCPC
Chief Executive Officer

OCF

TORONTO-BAYVIEW REGIONAL CANCER CENTRE

SUNNYBROOK HEALTH SCIENCE CENTRE



Chief Executive Officer:
- R.D.T. Jenkin, M.B.,B.S.

Radiation Oncologists:
- I. Ackerman, M.D.
- A.J. Dembo, M.B., B.Ch.
  Division Head
- J.M. Balogh, M.D.
- M.P. Berry, M.B.,B.S.
  (to Nov 30/90)
- P.A. Catton, M.D.
- M.A. Davey, M.D.
- M.A. Doherty, M.B.,B.S.
- G. Ege, M.D. (from Jan 1/91)
- R.G. MacKenzie, M.D.
- N.D. Mountifield, M.D.
- G.M. Thomas, M.D.
- R. Wong, M.D.
- C.S. Young, M.D.

Medical Oncologists:
- N.L. Berinstein, M.D.
- G. Bjarnason, M.D.
- R.A.A. Buckman, M.B., B.Ch.
- N.A. Iscoe, M.D.
- I.J. Kerr, M.D.
- N. Lassam, M.D.
- K.I. Pritchard, M.D.
  Division Head
- C.A. Sawka, M.D.
- D.J.A. Sutherland, M.D.

Gynecologic Oncology:
- A. Covens, M.D.
- D. De Petrillo, M.D.
  Division Head
- R. Osborne, M.D.

Clinical Assistants:
- W. Brown, M.D.
- P. Chart, M.D.
- R. Cragg, M.D.
- R. Haq, M.D.
- M. Horani, M.D.
- H.M. Kocandrle, M.D.
- L. Mulroy, M.D.
- C. Narayanan, M.D.
- J. Roseborough, M.D.
- J.M. Wall, M.D.

Physicists:
G. Doswell, M.Sc.
D. Mason, B.Sc.
P.F. O'Brien, M.Sc.
Division Head
N. Videla, Ph.D.
M. Woo, Ph.D.

Clinical Trials/Epidemiology:
G. DeBoer, Ph.D.
Division Head (from Jan 1/91)

Research:
R. Kerbel, Ph.D.
Division Head

Chief Operating Officer:
M. Moffat, M.H.Sc.

Assistant Administrator:
N. Lowe, M.H.Sc.

Administrative Assistant:
K.A. Nicholson

Finance Manager:
B. Copeland

Nurse Administrator:
L.J. Thompson, M.Sc.N.

Radiation Therapy Manager:
S.V. Scott, A.C.(T)

Health Information Services Manager:
M. Mistruzzi, C.C.H.R.A.(C)

Manager, Engineering Services:
B. Gillies

During 1990, the Toronto-Bayview Regional Cancer Centre (T-BRCC) struggled to adjust to major growth pressures. Phase I of the Centre's expansion program was completed and formally opened on Sept. 18, 1990. This expansion was made possible by a gift of $1 million from the citizens of North York and at the opening ceremonies Mayor Mel Lastman presented a cheque for this sum. This was also the last visit to the Centre of the Hon. Elinor Caplan in her role as Health Minister. This year major additions to our radiation facility came on line; these included an additional 6-MeV linear accelerator, a second simulator with a new two-simulator suite, new radiation treatment planning and review room, and a new mould room. By year's end we were treating daily approximately 190 patients by external beams. The Centre opened a new suite of offices and a meeting room for our social workers, psychologists, nutritionists, and pastoral care staff. We also have a new lecture theatre.

Detailed planning has continued for our major expansion on a new cancer patient accrual rate of 5000 per year. In May the Minister of Health approved $43 million for this expansion. We anticipate that construction will commence in the spring of 1991 and be complete by the end of 1993.

Dr. Robert Kerbel has been appointed Head of the Division of Cancer Research in Sunnybrook Health Science Centre's Reichmann Research Institute. Dr. Kerbel's team will occupy this new laboratory space in January 1991.

The clinical operation continues to expand. In 1990, the Centre established a new Division of Gynecological Oncology with, as its head, Dr. Denny De Petrillo; Drs. Ray Osborne and Al Covens also joined this Division. Our program of prevention and early diagnosis and our ability to provide multidisciplinary care in this area has been markedly enhanced by the addition of the colcoscopy suite. At the time of writing, we await the appointment of a full-time head of surgical oncology who will be funded by the Sunnybrook Health Science Centre (SHSC) but will have offices and other support in the T-BRCC.

Within the Provincial Breast Screening Program, T-BRCC will be responsible for screening approximately one-quarter of the eligible women in the province. The Scarborough screening centre opened in December and the North York will open in January 1991. A new diagnostic breast clinic, our first evening ambulatory care clinic, was opened at the Centre. The medical co-ordinator for this program is Dr. Pamela Chart.

In 1990, our Radiation Technology Training School graduated its first two trainees and both elected to join the staff of the Division of Radiotherapy. This school and its novel B.Sc. Training Program, which is expanding rapidly, has been authorized to enrol 12 students each year. This response to the critical shortage of radiation technologists ensures that we will be self-sufficient within five years.

At T-BRCC, during our rapid growth phase, the critical staff shortages have been in radiation oncologists, medical physicists and radiation technologists. At the time of writing, the shortage of radiation oncologists is the weakest link in our program; this shortage is the direct cause of waiting lists (for patients to be seen in consultation) as long as six to eight weeks, for breast cancer patients for example. During this year the Division of Radiation Oncology has been devastated as it watched Dr. Alon Dembo, the Division Head, fight his personal battle with acute leukemia.

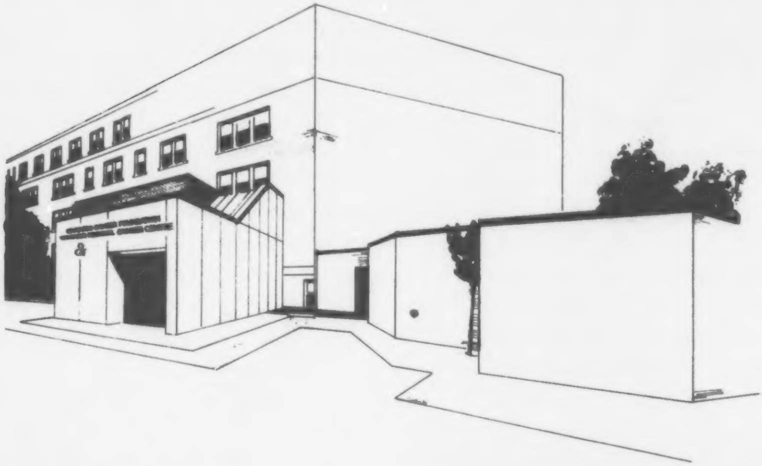
This year, Harold Wodinsky resigned as our Chief Operating Officer to take the challenge of senior Vice-President and Chief Operating Officer of the OCTRF. His replacement at T-BRCC is Malcolm Moffat, previously the Administrative Co-ordinator for the Department of Surgery at SHSC. In December, Dr. Gerrit DeBoer was appointed Head of the Division of Epidemiology and Clinical Trials for the comprehensive cancer program on this campus.

R.D.T. Jenkin, M.B.,B.S. FRCPC
Chief Executive Officer

OCTF

WINDSOR REGIONAL CANCER CENTRE

METROPOLITAN GENERAL HOSPITAL



Chief Executive Officer:
G.C.K. Mok, M.D.

Radiation Oncologists:
J.A. Gilchrist, M.B.,B.S.
(to Sept./90)
E. Laukkanen, M.D.
(from Nov./90)
L.F. Paszat, M.D.
C.D. Springer, M.B.,B.S.

Medical Oncologists:
H.T. Abu-Zahra, M.B., B.Ch.
Z.Y. Alam, M.B.
D.A. Sicheri, M.D.
S. Yoshida, M.D.

Physicists:
M. Gribble, M.Sc.
D. Smocovitis, M.Sc.

Chief Operating Officer:
J.G. Connors, M.H.S.A.

Manager, Financial Services:
E. Hancock

Head Nurses:
R.A. Girard, Reg.N.
S. Vickers, Reg.N.

Manager, Radiation Therapy:
M. Rice, A.C.(T)

Manager, Computer Services
N. Tiltman

Manager, Health Information Services:
R. Kavanaugh

The number of physicians in the Windsor Regional Cancer Centre—four medical oncologists and four radiation oncologists—has remained fairly constant over the past two years. At the end of August of this year, Dr. James Gilchrist, a radiation oncologist, returned to the London Regional Cancer Centre. Dr. Ethan Laukkanen filled this position in November. In September, Mr. John Connors, a professional health-care administrator, joined the Windsor Centre as Chief Operating Officer.

The Windsor Regional Cancer Centre Radiation Therapy Technologist School opened in August 1988. Earlier this year, following an on-site accreditation visit, we were awarded a five-year accreditation certificate. Our first class celebrated their graduation in mid-August of this year. Both male students have written their Board examinations and have accepted conditional job offers with our Centre. Currently we have one second-year student and two first-year students.

In an effort to increase the RTT training output, the teaching staff in the London and Windsor Centres are cooperating on a plan to combine the training resources of both centres.

We were able to take out-of-town referrals to help ease the backlog of patients awaiting radiation therapy in the fall of 1989. During the past 12 months, we have treated a number of patients from Metropolitan Toronto and recently from the Hamilton area.

Relations between the Centre and the Canadian Cancer Society (CCS) have grown even stronger with the arrival of their new Essex County District Director and her assistant—Mrs. Brenda McConnoll and Mr. Michael Clark. A liaison committee, formed to facilitate co-operation between the Centre, the Hospice of Windsor, the CCS and the Victoria Order of Nurses has proven very productive. More than one-half of our physicians are members of the District or Unit Boards of the CCS, acting in the capacity as medical advisors.

Earlier this year, we were authorized to purchase a new simulator to replace the 15-year-old unit. We commissioned this machine in October.

We are in the process of establishing a breast screening clinic in Windsor, which we hope will be open for screening in late winter.

Our architect is completing the final drawings for the Centre's renovation and expansion. We hope to have the project ready for the Ministry of Health's approval and for tender early in the new year. This expansion is a "quick fix" solution to provide space for the "existing" Health Record

Department, Business Office, Information Services, Clinical Trials Protocol Office, Library and Meeting Room, and Medical Oncology treatment area. The total area for outpatient services will be only minimally sufficient for the next four to five years.

Windsor experienced a 5% increase of all new cases in 1989 and this level of increase is being maintained in the first eight months of 1990. With this continued growth in patient numbers, the need for patient services, both in terms of high-energy machines and service space, may exceed what we have to offer by 1994-1995. By then, we will have to have new machines and more clinic space.

G.C.K. Mok, M.D.
Chief Executive Officer

SERVICE LOAD

The following tables describe the service load of the Foundation's eight regional cancer centres during the calendar year 1989.

In 1989, 57,968 patients were seen at these centres. Of these, 93% had malignant lesions and, of these lesions, 17,216 were new to the centres (Table I). Of cases referred for non-malignant conditions, 76% were first seen in 1989 (Table II). The majority of the non-malignant conditions were seen for follow-up and consultation (1,529 and 594 respectively). In all, 12,619 malignant cancer cases were treated by radiotherapy (Table III); of these, 5,655 were treated by cobalt units, 6,035 by a linear accelerator, and 929 by other methods of radiotherapy.

During the year, patients made 588,691 visits to the regional cancer centres and the majority, 574,655, were for treatment of malignant disease (Table IV). Of all radiation treatments, 91% were given on an outpatient basis (Table V).

As of January 1, 1982, with the implementation of the Patient Care Management System (PCMS) in the centres, it has been possible to retrieve data in more detail than was possible in previous years. The current tabulations are taken from data as of August 1990. Consultation and follow-up visits have been divided and appear in separate columns in Tables I,II and IV. Simulations are shown in Table V but are not included in the totals. It must be emphasized that these tables are comparable only with the service load tables published for 1982 to 1988 inclusive; they are not comparable with those for the years before PCMS was implemented.

TABLE I
Malignant Caseload During 1989*

TREATMENT CENTRE	TREATED				Consultation Only	Follow-up Only	TOTAL
	Radiation	Radiation and Chemo-therapy	Chemo-Therapy	Procedures			
	Cases New in Current Year						
Hamilton	1,089	274	575	31	675	877	3,521
Kingston	494	127	193	14	265	329	1,422
London	1,044	333	452	68	529	807	3,233
Ottawa	1,174	307	523	117	385	782	3,288
Sudbury	0	0	231	8	126	130	495
Thunder Bay	215	89	117	7	76	114	618
Toronto-Bayview	1,358	182	259	322	528	767	3,416
Windsor	399	115	203	27	148	331	1,223
TOTAL	5,773	1,427	2,553	594	2,732	4,137	17,216
	Cases Registered in any Previous Year						
Hamilton	510	355	1,302	32	322	5,509	8,030
Kingston	177	94	324	39	129	2,490	3,253
London	401	255	713	158	176	4,614	6,317
Ottawa	385	423	1,161	154	127	6,449	8,699
Sudbury	0	0	300	33	6	353	692
Thunder Bay	72	57	203	24	50	1,111	1,517
Toronto-Bayview	410	100	188	171	53	3,751	4,673
Windsor	107	115	460	65	75	2,453	3,275
TOTAL	2,062	1,399	4,651	676	938	26,730	36,456
TOTAL ALL MALIGNANT	7,835	2,826	7,204	969	1,122	30,867	53,672

*Includes cases seen at peripheral clinics.

TABLE II
Other (Non-Malignant) Caseload During 1989*

TREATMENT CENTRE	TREATED				Consultation Only	Follow-up Only	TOTAL
	Radiation	Radiation and Chemo-therapy	Chemo-Therapy	Procedures			
	Cases New in Current Year						
Hamilton	47	2	68	12	116	287	532
Kingston	5	0	30	78	106	268	487
London	29	2	58	336	98	203	726
Ottawa	28	0	4	164	23	107	326
Sudbury	0	0	3	1	5	20	29
Thunder Bay	4	0	13	16	55	132	220
Toronto-Bayview	17	0	9	150	143	280	599
Windsor	4	0	22	55	48	232	361
TOTAL	134	4	207	812	594	1,529	3,280
	Cases Registered in any Previous Year						
Hamilton	3	0	0	1	2	29	35
Kingston	1	0	1	1	1	27	31
London	0	1	2	5	4	42	54
Ottawa	2	1	2	14	1	88	108
Sudbury	0	0	1	0	0	0	1
Thunder Bay	0	0	1	0	0	13	14
Toronto-Bayview	3	0	0	65	11	643	722
Windsor	0	0	4	1	3	43	51
TOTAL	9	2	11	87	22	885	1,016
TOTAL ALL MALIGNANT	143	6	218	899	616	2,414	4,296

*Includes cases seen at peripheral clinics.

TABLE III
Cases Treated During 1989 by Method of Radiotherapy

METHOD OF TREATMENT	HAMILTON	KINGSTON	LONDON	OTTAWA	THUNDER BAY	TORONTO BAYVIEW	WINDSOR	TOTAL
	Malignant Neoplasms							
Superficial x-ray	128	186	–	30	16	43	90	493
Deep x-ray	–	–	–	–	–	–	–	0
Cobalt^{60}	1,579	211	730	1,365	206	1,133	432	5,656
Cesium^{137}	–	–	–	–	–	–	–	0
Betatron	–	–	–	–	–	–	–	0
Linear accelerator	816	628	1,705	1,208	280	1,094	304	6,035
Intracavitary	61	21	93	48	5	63	17	308
Interstitial	8	3	5	100	–	4	–	120
Moulds and applicators	–	–	1	–	–	–	–	1
Systemic isotopes	–	–	–	–	–	–	–	0
Others*	1	1	–	4	–	–	–	6
SUB-TOTAL	2,593	1,050	2,534	2,755	507	2,337	843	12,619
Simulations	2,970	1,003	3,440	3,246	566	2,553	1,708	15,486
	Other Non–Malignant							
Superficial x-ray	2	1	–	–	–	–	–	3
Deep x-ray	–	–	–	–	–	–	–	0
Cobalt^{60}	34	1	4	17	1	6	3	66
Cesium^{137}	–	–	–	–	–	–	–	0
Betatron	–	–	–	–	–	–	–	0
Linear accelerator	15	4	19	15	4	14	1	72
Intracavitary	–	–	–	–	–	–	–	0
Interstitial	–	–	–	–	–	–	–	0
Moulds and applicators	–	–	10	–	–	–	–	10
Systemic isotopes	–	–	–	–	–	–	–	0
Others*	–	–	–	–	–	–	–	0
SUB-TOTAL	51	6	33	32	5	20	4	151
Simulations	61	5	36	75	7	18	6	208
TOTAL**	2,644	1,056	2,567	2,787	512	2,357	847	12,770

* Others include radiation codes unknown.

** A case can be treated by more than one method per year. Simulations are displayed but are not included in the totals.

TABLE IV
Service Load, 1989

TREATMENT CENTRE	TREATMENT			NON-TREATMENT			TOTAL
	Radiation	Chemo-therapy	Procedures	Simulations	*Consul-tations	Follow-up Visits	
	Visits for Malignant Neoplasms						
Hamilton	31,510	18,060	285	2,970	5,930	39,247	98,002
Kingston	12,526	3,840	836	1,003	2,161	23,041	43,407
London	37,867	8,899	1,670	3,440	5,216	43,312	100,404
Ottawa	41,783	17,682	2,247	3,246	4,037	74,822	143,817
Sudbury	0	4,539	698	0	530	17,671	23,438
Thunder Bay	9,537	3,561	473	566	1,078	10,991	26,206
Toronto-Bayview	33,632	4,314	1,046	2,553	4,012	37,071	82,628
Windsor	13,222	6,919	3,528	1,708	1,837	29,539	56,753
TOTAL	180,077	67,814	10,783	15,486	24,801	275,694	574,655
	Other Non-Malignant						
Hamilton	498	227	42	61	313	928	2,069
Kingston	69	81	402	5	301	1620	2,478
London	352	123	705	36	300	947	2,463
Ottawa	399	92	311	75	122	666	1,665
Sudbury	0	11	17	0	15	183	226
Thunder Bay	82	68	64	7	165	515	901
Toronto-Bayview	209	14	254	18	548	1,280	2,323
Windsor	37	110	181	6	292	1,285	1,911
TOTAL	1,646	726	1,976	208	2,056	7,424	14,036
TOTAL ALL VISITS	181,723	68,540	12,759	15,694	26,857	283,118	588,691

* Consultations includes re-consultations.

TABLE V

Treatments by Radiotherapy during 1989, In-Patients and Out-Patients

METHOD OF TREATMENT	HAMILTON		KINGSTON		LONDON		OTTAWA		THUNDER BAY		TORONTO BAYVIEW		WINDSOR		TOTAL	
	In	Out	In	Out	In	Out	In	Out	In	Out	In	Out	In	Out	In	Out
	Malignant Neoplasms															
Superficial x-ray	10	900	39	917	–	–	5	217	–	149	–	313	4	683	58	3,179
Deep x-ray	–	–	–	–	–	–	–	–	–	–	–	–	–	–	0	0
Cobalt^{60}	958	15,387	231	2,949	2,296	4,022	2,324	18,038	685	3,449	1,291	11,595	1,023	4,965	8,808	60,405
Cesium^{137}	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Betatron	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Linear accelerator	371	13,813	767	7,585	2,985	28,454	1,393	19,644	473	4,774	725	19,639	287	6,241	7,001	100,150
Intracavitary	61	–	25	–	102	–	56	–	7	–	65	–	19	–	335	0
Interstitial	8	–	3	–	1	6	102	–	–	–	4	–	–	–	118	6
Moulds and applicators	–	–	–	–	–	1	–	–	–	–	–	–	–	–	0	1
Systemic isotopes	–	–	–	–	–	–	–	–	–	–	–	–	–	–	0	0
Others	2	–	–	10	–	–	4	–	–	–	–	–	–	–	6	10
SUB-TOTAL	1,410	30,100	1,065	11,461	5,384	32,483	3,884	37,899	1,165	8,372	2,085	31,547	1,333	11,889	16,326	163,751
Simulations	218	2,752	140	863	779	2,661	518	2,728	109	457	226	2,327	204	1,504	2,194	13,292
	Other Non–Malignant															
Superficial x-ray	–	6	–	3	–	–	–	–	–	–	–	–	–	–	0	9
Deep x-ray	–	–	–	–	–	–	–	–	–	–	–	–	–	–	0	0
Cobalt^{60}	–	257	–	5	–	13	–	148	–	20	2	38	–	32	2	513
Cesium^{137}	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Betatron	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Linear accelerator	–	235	37	24	30	299	–	251	–	62	–	169	–	5	67	1,045
Intracavitary	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Interstitial	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Moulds and applicators	–	–	–	–	–	10	–	–	–	–	–	–	–	–	0	10
Systemic isotopes	–	–	–	–	–	–	–	–	–	–	–	–	–	–	0	0
Others	–	–	–	–	–	–	–	–	–	–	–	–	–	–	0	0
SUB-TOTAL	0	498	37	32	30	322	0	399	0	82	2	207	0	37	69	1,577
Simulations	0	61	2	3	1	35	–	75	–	7	0	18	–	6	3	205
TOTAL	1,410	30,598	1,102	11,493	5,414	32,805	3,884	38,298	1,165	8,454	2,087	31,754	1,333	11,926	16,395	165,328

**Others include radiation codes unknown.

CONSULTATIVE AND FOLLOW-UP CLINICS

The distribution of these clinics reflects the general zones of service of the Foundation's Regional Cancer Centres in Hamilton, Kingston, London, Ottawa, Sudbury and Thunder Bay; and of the Princess Margaret Hospital, Toronto.

HAMILTON

Brantford	St. Joseph's Hospital
Burlington	Joseph Brant Memorial Hospital
Cambridge (Galt)	Cambridge Memorial Hospital
Guelph	Guelph General Hospital
Hamilton	McMaster Medical Centre and St. Joseph's Hospital
Niagara Falls	Greater Niagara General Hospital
St. Catharines	Hotel Dieu Hospital
Welland	Welland County General Hospital

KINGSTON

Peterborough	St. Joseph's Hospital
Trenton	Trenton Memorial Hospital

LONDON

Chatham	Public General Hospital
Kitchener	Kitchener-Waterloo Hospital
London	St. Joseph's Health Centre
Owen Sound	Grey-Bruce Regional Health Centre
Sarnia	St. Joseph's Hospital and Sarnia General Hospital
St. Thomas	St. Thomas-Elgin Hospital
Stratford	Stratford General Hospital
Wingham	Wingham and District Hospital
Woodstock	Woodstock General Hospital

OTTAWA

Cornwall	Cornwall General Hospital and Hotel Dieu Hospital
Ottawa	Riverside Hospital, Montfort Hospital and Queensway-Carleton Hospital
Pembroke	Pembroke Civic Hospital

SUDBURY

North Bay	North Bay Civic Hospital

THUNDER BAY

Atikokan	Atikokan General Hospital
Dryden	Dryden District General Hospital
Fort Frances	La Verendrye General Hospital
Geraldton	Geraldton District Hospital
Hearst	Notre-Dame Hospital
Sioux Lookout	Sioux Lookout General Hospital
Terrace Bay	McCausland Hospital

TORONTO

Sault Ste. Marie	Plummer Memorial Public Hospital
Timmins	St. Mary's Hospital

CLINICAL CONSULTANTS AT THE OCTRF REGIONAL CANCER CENTRES AND THE PRINCESS MARGARET HOSPITAL

(As at December 31, 1990)

OCF Hamilton Centre:

M. Ali, M.D.
S. Archibald, M.D.
A.M. Benger, M.D.
W.F. Bennett, M.D.
I.W. Blackstone, M.D.
M. Brain, M.D.
A.J. Campbell-Moscrop, M.D.
B. Clark, M.D.
D. Clark, M.D.
J. Collins, M.D.
I.R. Davis, M.D.
P.B. Dent, M.D.
R. deVilliers, M.D.
B. Findlay, M.D.
J.D. Gowing, M.B.,B.S.
R.A. Hadden, M.D.
J. Harvey, M.D.
D.A. Hitch, M.D.
B.S. Jackson, M.D.
P. Jenkin, M.D.
J. Kearns, M.D.
P. Knight, M.B.,Ch.B.
J.A. McBride, M.B.,Ch.B.
R. Meyer, M.D.
W. Nicholson, M.D.
S.E. O'Brien, M.D.
W.L. Orovan, M.D.
J.E. Paulseth, M.D.
M. Rathbone, M.D.
W.D. Rider, M.B.,Ch.B.
J.T. Roberts, M.B.,Ch.B.
D. Rosenthal, M.D.
D. Sauder, M.D. (to Sept/90)
D. Savelli, M.D.
B. Trossman, M.D.
P. Vasarinsh, M.D.
I. Walker, M.D.
J. Weitz, M.D.
W.E.C. Wilson, M.D.
C. Woolever, M.D.
J.E.M. Young, M.D.

OCF Kingston Centre:

J.M. Blakeman, M.D.
H. Brown, M.D.
S.C.P. Bryson, M.D.
J.A. Carmichael, M.D.
W.E.N. Corbett, M.D.
D. Dexter, M.D.
B.E. Elliott, Ph.D.
H.B. Dinsdale, M.D.
S.F. Hall, M.D.
J.W. Kerr, M.D.
K.W. Mackie, M.D.
J. Matthews, MRCP, MRCLP
D. McIntosh, M.D.
R.J. Riopelle, M.D.
D.M. Robertson, M.D.
M. Silva, M.D.
H.D. Steele, M.D.
E.E. Sterns, M.D.
K. Taguchi, M.D.
D.M.L. Williams, M.D.

OCF London Centre:

H.H. Allen, M.D.
W.B. Barton, M.D.
R.M. Barr, M.D.
U. Bite, M.D.

W. Brien, M.D.
A.E. Cairney, M.D.
M. Carey, M.D.
J. Chertkow, M.D.
J. Chin, M.D.
I. Chin Yee, M.D.
J. Coles, M.D.
R.F. Del Maestro, M.D.
G. DeRose, M.D.
L.L. deVeber, M.D.
A.A. Driedger, M.D.
J. Duff, M.D.
K. Elsevich, M.D.
M. Girotti, M.D.
D. Girvan, M.D.
J. Gonder, M.D.
R.W. Gottschalk, M.D.
L.C. Guenther, M.D.
J. Harris, D.D.S.
H. Heeneman, M.D.
R.L. Holliday, M.D.
R. Inculet, M.D.
M.J. Inwood, M.D.
M.E. Kirk, M.D.
H.Lampe, M.D.
F. Lefcoe, M.D.
D. Macdonald, M.D.
L. McCurdy, M.D.
R.M. McFarlane, M.D.
T.D. McLarty, M.D.
L.R. McWhinney, M.D.
E. Meads, M.D.
D.B. Meltzer, M.D.
D. Moulin, M.D.
J. Nisker, M.D.
J. Powe, M.D.
J.F. Sangster, M.D.
I.D.F. Schofield, D.D.S.
R. Shearer, M.D.
A. Smith, M.D.
K. Sparrow, M.D.
W.K. Stavraky, M.D.
B. Taylor, M.D.
R. Thomas, M.D.
D.M. Wexler, M.D.
J. Wyatt, M.D.

OCF Ottawa Centre:

G. Allen, M.D.
J.W. Atkinson, M.D.
L.I. Avruch, M.D.
G.G. Barber, M.D.
P.T. Barron, M.B.,Ch.B.
A.W. Barry, M.D.
J.M. Belanger, M.D.
D.N. Bell, M.D.
M. Bell, M.D.
P. Benoit, M.D.
R.J. Benzie, M.D.
J.M. Beresford, M.B.,Ch.B.
J. Bormanis, M.D.
A.G. Bouchard, M.D.
L. Busque, M.D.
L.J. Byford, M.D.
S. Chater, M.D..
C.K. Chew, M.D.
J.M. Cowan, M.B.,Ch.B.
J. Cox, M.D.
A. Crepeau, M.D.
M. Curran, M.D.
V. Da Silva, M.D.
Y. de la Bastide, L.R.C.P.(U.K.)
J.J. Deneault, M.D.
J.E. Devitt, M.D.
J. Drouin, M.D.
M.J. Duncan, M.D.
L. Eidus, M.D.
R. Elliott, M.D.
R.J. Fairful-Smith, M.B.,Ch.B.
M. Finkelstein, M.D.

J.B. Freeman, M.D.
G. French, M.D.
N.G. Futter, M.D.
G. Garber, M.D.
L. Garnett, M.D.
E. Gear, M.D.
J. Gerin-Lajoie, M.D.
A. Giachino, M.D.
R.R. Gillies, M.D.
Z. Grahovac, M.D.
J.E. Green, M.D.
P. Hamilton, M.D.
D.I. Hammond, M.D.
A. Haq, M.D.
R. Heringer, M.D.
D.P. Hill, M.D.
R.B. Hladkowicz, M.D.
R.V. Hodder, M.D.
E. Hsu, M.D.
L.B. Huebsch, M.D.
H. Hugenholtz, M.D.
J.B. Hurtig, M.D.
R. Jackson, M.D.
T.G. Jones, M.B.,B.S.
J. Kitts, D.D.S.
A. Lamothe, M.D.
B.M. Lefebvre, M.D.
G.N. Lewis, M.D.
B. Luke, M.D.
N. Lui, M.D.
P.C. MacEwen, M.D.
J.P. MacLeod, M.D.
F. Mai, M.D.
K.T. Mai, M.D.
S. Markman, M.D.
R. Martineau, M.D.
N. Mayer, M.D.
R.W. McIntyre, M.D.
W.A. McLeish, M.D.
D.E. McKay, M.D.
J. McKenna, M.D.
S. Mercer, M.D.
N.Z. Mikhael, M.D.
D. Miller, M.D.
V. Monpetit, M.D.
D. Moors, M.D.
M. Navarro, M.D.
K. Nolan, M.D.
P.F. Odell, M.D.
A. Peloquin, M.D.
J.P. Penning, M.D.
M. Prefontaine, M.D.
D.N. Preston, M.D.
P. Rasuli, M.D.
G. Reid, M.D.
R.N. Rivington, M.D.
O.P. Rosaeg, M.D.
H.J. Sachs, M.D.
B. Samson, M.D.
J.F. Scott, M.D.
J. Seely, M.D.
F.M. Shamji, M.D.
D.S. Skene, M.D.D.
G. Skidmore, M.D.
P. Sullivan, M.D.
J.R. Taylor, M.D.
E.N. Thompson, M.D.
T. Todd, M.D.
M. Tousignant, M.D.
L.G. Van Wyck, M.D.
W.G. Walsh, M.D.
C. Watters, M.D.
L. Weatherhead, M.D.
K.B. Wilson, M.D.
R.W. Yarnell, M.D.

OCF Sudbury - Northeastern Ontario Regional Cancer Centre:

J. Abourbih, M.D.
R. Bergh, M.D.

J.M. Dahmer, M.D.
J.F. D'Aloisio, M.D.
G. Helie, M.D.
V. Kumar, M.D.
J. Mazurka, M.D.
R. Odhiambo, M.D.
A. Ogundimu, M.D.
L.Q. Wong, M.D.

OCF Toronto-Bayview Centre:

J.D. Anderson, M.D.
D. Assaad, M.D.
R.S. Bell, M.D.
B.D. Birt, M.B.,B.S.
T.D.R. Briant, M.D.
G. Bradley, M.D.
P.L. Chan, M.D.
D.H. Cowan, M.D.
G.M. Davies, M.B., B.Ch.
H.R. Dawson, M.D.
C. De Angelis, Pharm.D.
M. Fazl, M.D.
L. From, M.D.
R. Gilbert, M.D.
L.T. Glickman, M.D.
S. Hanna, M.B., B.Ch.
A.W. Harrison, M.D.
S. Huang, M.D.
J. Hurwitz, M.D.
J.A. Jambrosik, M.D.
N.A. Kerenyi, M.D.
L. Klotz, M.D.
A. Kolin, M.D.
A.J. Lewis, M.D.
J.H.P. Main, D.D.S.
M.A. McKenzie, M.D.
H.A.B. Miller, M.B.,B.S.
T. Mok, M.D.
I. Morova-Protzner, M.D.
J.F. Murray, M.D.
B.Y. Ngan, M.D.
J.H. Phillips, M.D.
P.H. Pinkerton, M.D.
E.R. Pohlman, M.D.,C.M.
P. Poldre, M.D.
S.V. Pollack, M.D.
Y. Rahim, M.D.
M.D.O. Reis, M.D.
B.P. Rosen, M.D.
D.W. Rowed, M.D.
M.L. Schwartz, M.D.
J.L. Semple, M.D.
J.S. Senn, M.D.
P.A. Shaw, M.D.
B. Sheridan, M.B.,B.S.
P.K. Shuen, M.D.
J.R. Srigley, M.D.
S.E. Sutherland, M.D.
G.A. Taylor, M.D.
M. Tile, M.D.
M.E. Tweeddale, M.D.
B.C. Walters, M.D.
P.M. Webster, M.D.

The Princess Margaret Hospital, Toronto:

P.W. Alberti, M.B.,B.S.
U. Ambus, M.D.
J.D. Anderson, D.D.S.
A.G. Andrews, D.D.S.
A.G. Awad, M.D.
M.A. Baker, M.D.
J.L.M. Bean, M.D.
R.S Bell, M.D.
M. Bernstein, M.D.
N. Bharatwal, M.D.
M.E. Blackstein, M.D.
J.M.A. Bohnen, M.D.
J.B. Boyd, M.D.
G. Bradley, D.D.S.

T.D.R. Briant, M.D.
D. Brown, M.D.
A.W. Bruce, M.B.,Ch.B.
D.P. Bryce, M.D.
C.B. Bubela, M.D.
M.B. Buckspan, M.D.
M. Bulbul, M.D.
J.J. Caesar, M.D.
H.S.L. Chan, M.B.,B.S.
A.W. Chisholm, M.D.
D.B. Clark, M.D.
J.G. Connolly, M.D.
D.H. Cowan, M.D.
J.S. Crawford, M.D.
P.L. Darby, M.B.,B.S.
A.D. DePetrillo, M.D.
C. Derzko, M.D.
L.G. Douglas, M.D.
I. Dube, Ph.D.
R. Dymond, M.D.
W.M. Easterbrook, M.D.
R.J. Evans, M.D.
M. Fanning, M.D.
B.J.J. Fernandes, M.D.
R.M. Filler, M.D.
E.B. Fish, M.D.
B.K. Fisher, M.D.
J.A. Fisher, M.D.
J.L. Freeman, M.D.
B.L. Gallie, M.D.
W.O. Geisler, M.D.
A.H. Gerulath, M.D.
C.M. Godfrey, M.D.
M. Goldberg, M.D.
P.J. Goodwin, M.D.
D.A. Gordon, M.D.
P. Gullane, M.B., B.Ch.
G.B. Haber, M.D.
J.A. Hakes, M.B.,Ch.B.
M.L. Halperin, M.D.
W.J. Hannah, M.D.
G.D. Hart, M.D.
R.H.A. Haslam, M.D.
D.E. Hastings, M.D.
C. Hegarty, M.B., B.Ch.
C.H. Hollenberg, M.D.
R. Hopkins, D.D.S.
N.S. Hradsky, M.D.
M.A. Hutcheon, M.D.
R.H. Hyland, M.D.
C.G. Jamieson, M.B.,B.S.
S.E. Jelenich, M.D.
R.D.T. Jenkin, M.B.,B.S.
M.A. Jewett, M.D.
D.P. Jones, M.D.
A.S. Katz, M.D.
M. Kazden, M.D.
A.G. Keresteci, M.D.
D.W. Killinger, M.D.
M.H. King, M.D.
C. Kotwall, M.D.
B. Langer, M.D.
F. Langer, M.D.
V.G. Lawson, M.D.
L. Lee, M.D.
G.M. Lickrish, M.B.,Ch.B.
F.H. Lowy, M.D.
W.J.C. MacArthur, M.D.
R.D. MacDonald, M.D.
T.A. MacKenzie, M.D.
L.J. Mahoney, M.D.
J.H.P. Main, D.D.S.
N.E. Marcon, M.D.
A.G. Matlow, M.D.
R.J. McBroom, M.D.
D. McCready, M.D.
J.S. McGrail, M.D.
J.W. Meakin, M.D.
W.G. Middleton, M.D.
C.B. Mortimer, M.D.

P.J. Muller, M.D.
J.K. Murphy, M.D.
T.M. Murray, M.D.
R.A. Mustard, Jr., M.D.
R.E. Myers, M.D.
R.J. Osborne, M.D.
F.R. Papsin, M.D.
G.A. Patterson, M.D.
C. Pavlin, M.D.
F.G. Pearson, M.D.
R.G. Perrin, M.D.
D.G. Potts, M.D.
K. Pritchard, M.D.
K.P. Pritzker, M.D.
K. Psihramis, M.D.
C.A. Ramsay, M.D.
J.T. Rankin, B.M., B.Ch.
B. Rosen, M.D.
I.B. Rosen, M.D.
L. Rotstein, M.D.
J.S. Senn, M.D.
S. Sidlofsky, M.D.
M.D. Silver, M.D.
E.R. Simpson, M.D.
H.S. Smyth, M.D.
H.A. Smythe, M.D.
M.L. Soots, M.D.
A.H. Squires, M.D.
H.S. Stern, M.D.
R.M. Stone, M.D.
P. Straka, M.B.,Ch.B.
D.J. Sutherland, M.D.
J.O. Swales, M.D.
J.M. Symington, B.D.S.
H. Tanzer, M.D.
S.A.P. Tindal, M.B.,Ch.B.
J. Trachtenberg, M.D.
M.L.S. Vachon, Ph.D.
R. Volpe, M.D.
C.P.N. Watson, M.D.
G.D. Webb, M.D.
R.H. Wilkinson, M.D.
T. Winton, M.D.
L. Wright, Ph.D.
F.R.H. Wrigley, M.B.,B.S.
A. Zipursky, M.D.
R.M. Zuker, M.D.

THE ONTARIO CANCER INSTITUTE

THE ONTARIO CANCER INSTITUTE

incorporating

THE PRINCESS MARGARET HOSPITAL

D.R. Carlow, M.D.
President and Chief Executive Officer
500 Sherbourne St.
Toronto, Ontario M4X 1K9
Tel: (416)924-0671

Medical Oncology:

D.E. Bergsagel, M.D.*
N.F. Boyd, M.B.,B.S.
J.E. Curtis, M.D.
M. Elliott, M.D.
C. Erlichman, M.D.
R. Feld, M.D.
R. Hasselback, M.D.,C.M.
J. Lipton, M.D.
J.M. Meharchand, M.B.,Ch.B.
H.A. Messner, M.D.
M.D. Minden, M.D.
M. Moore, M.D.
I.C. Quirt, M.D.
J.F.G. Sturgeon, M.B.,B.S.
I.F. Tannock, M.D., Chief
D. Warr, M.D.

Radiation Oncology:

R. Bissett, M.D.**
R.S. Bush, M.D.***
C.N. Catton, M.D.
R.M. Clark, M.B.,B.S.
B.J. Cummings, M.B.,Ch.B.
W. Duncan, M.B.,Ch.B.**
A. Fyles, M.D.
M.K. Gospodarowicz, M.D.
T.J. Keane, M.B.,B.Ch., Chief
N.J. Laperriere, M.D.
P.D. Lefebvre, M.D.**
W. Levin, M.B.,Ch.B.
F.F. Lui, M.D.
L. Manchul, M.D.
M. McLean, M.B.,B.Ch.
A.J. Munro, M.B.,Ch.B.**
B. O'Sullivan, M.B.,B.Ch.
D.G. Payne, M.D.
J.F. Pringle, M.B.,Ch.B.
G.A. Rawlings, M.D.
W.J. Simpson, M.D.
S.B. Sutcliffe, M.D.
R. Tsang, M.D.
P. Warde, M.B.,B.Ch.
W. Wells, M.D.
S. Wong, M.D.
J.L. Yeoh, M.D.

Dentistry:

W.G. Maxymiw, D.D.S., Chief
R.E. Wood, D.D.S.

Diagnostic Imaging:

R. Blend, M.B.,B.S.
Acting Head
R. Goldberg, M.D.
S. Herman, M.D.
R. Peto, M.D.

Nuclear Medicine:

I. Boxen, M.D.
Division Head

Pathology:

V.L. Fornasier, M.D.
V. Jay, M.B.,B.S.
G.J. Laroye, M.D.
N. Miller, M.D.
B.J. Patterson, M.D.
H. Richmond, M.B.,Ch.B.
Acting Head
T. Treger, M.D.

Microbiology:

D. Low, M.D., Chief
A. McGeer, M.D.
A. Simor, M.D.
P.G. Tuffnell, M.D.*

RESEARCH:

Structural and Molecular Biology:

J. Gariepy, Ph.D.
R. Gronostajski, Ph.D.
V. Ling, Ph.D.
Division Head
F.P. Ottensmeyer, Ph.D.

Cell/Molecular Biology:

S. Benchimol, Ph.D.
N. Iscove, Ph.D.
T.W. Mak, Ph.D.
E.A. McCulloch, M.D.
Division Head
H. Messner, M.D.
R.G. Miller, Ph.D.
M.D. Minden, M.D.
C. Paige, Ph.D.
N. Miyamoto, Ph.D.

Epidemiology and Statistics:

N. Boyd, M.D.
Division Head
R. Bruce, Ph.D.
A.J. Cunningham, Ph.D.
H. Llewellyn-Thomas, Ph.D.**
S. Minkin, Ph.D.
J.E. Till, Ph.D.
D. Tritchler, Ph.D.

Experimental Therapeutics:

C. Erlichman, M.D.
D.W. Hedley, M.B.,Ch.B.
R.P. Hill, Ph.D.
J.W. Hunt, Ph.D.
A.M. Rauth, Ph.D.
G.F. Whitmore, Ph.D.
Division Head

Clinical Physics:

H. Alasti-Hamed, M.Sc.
S. Beddar, Ph.D.
F. Cheung, Ph.D.
D.M. Galbraith, B.Sc.
J. Grant, M.Sc.
M. Islam, Ph.D.
B. Japp, B.Sc.
J. Jezioranski, M.Sc.
P.M.K. Leung, Ph.D.
M. Lumley, M.Sc.
C. Mah, M.Sc.
B. McParland, Ph.D.
A. Mosseri, M.Sc.
M. Nikolic, Ph.D.
J.A. Rawlinson, M.Sc.
S. Rose, M.Eng.
M. Sherar, Ph.D.
C. Thomason, Ph.D.
J. Van Dyk, M.Sc.
Y. Zhu, Ph.D.

Imaging:

M.J. Bronskill, Ph.D.**
S. Foster, Ph.D.
Division Head**
R.M. Henkelman, Ph.D.**
D. Plewes, Ph.D.**
M. Yaffe, Ph.D.**

M.C. Archer, Ph.D.

ADMINISTRATION:

Vice-Presidents:

J. Beed, M.Sc.N.
Patient Care
R. Buick, Ph.D.
Research

C. Charlton, M.A.
Resource Development**
E. Govoni, C.A.
Finance
A. Headricks, M.A.
Human Resources
J.P. Holder, B.Sc.N.
Nursing**
J.E. Ratz, B.A.
Planning and
Hospital Services*
S. B. Sutcliffe, M.D.
Oncology Programs
T. Warner, S.M.
Quality and Utilization
Management

Assistant Vice-Presidents:
T.J.D. West, B.A.
Medical Administration
W. Wilkinson
Support Services

Manager of Health Records:
A. Buchanan, C.C.H.R.A.(C)

Librarian:
C. Morrison, M.L.S.

*Retired during 1990
**Left during 1990
***Died during 1990

My report for Cancer In Ontario 1989 expressed concern about the negative impact on patient care of significant shortages of staff, particularly in radiation therapy and nursing. This year I am pleased to report that 1990 was highlighted by the successful recruitment from around the world of many new staff to this organization. Waiting times to begin radiation therapy improved, the 10th radiation therapy machine at the main hospital was brought into service and our ability to provide care for patients has significantly improved.

In February 1990, we began construction of a satellite radiation therapy unit in the basement of Mount Sinai Hospital and it is scheduled to open in April 1991. This satellite with its four linear accelerators is phase I of the new University Avenue hospital and eventually will be linked to the main hospital when it is completed early in 1995.

We are pleased to report significant progress towards the day when the shovel goes in the ground to start construction of the new hospital. In the fall of 1990, a change of government resulted in some delays, but, on the last day of 1990, ownership of the land at 610-620 University Avenue was transferred to OCI/PMH. We will now be able to proceed with obtaining the necessary construction permits from the City of Toronto before going to tender in the spring.

In 1990 changes to the Ministry of Health's provincial funding strategy for the cancer system created complications for the Ontario Cancer Control Fund. In 1990, this fundraising partnership between OCI/PMH, OCTRF and the Canadian Cancer Society Ontario Division was dissolved and the funds raised to that date were transferred to the separate organizations according to agreements between the three parties and the donors. The Princess Margaret has established its own capital campaign under the chairmanship of Mr. Tony Fell, President and CEO of RBC Dominion Securities Inc. This campaign will be launched in late 1991 to raise $50 million towards the cost of building and equipping the new OCI/PMH.

At the end of 1990, the hospital underwent accreditation by the Canadian Council on Hospital Accreditation and received a two-year award. Because the surveyors commended the patient-care programs and initiatives, the award may be upgraded to three years upon completion of some recommended administrative changes such as updating bylaws. We had withheld changes to these bylaws pending finalization of the Ontario Cancer Control Agency (OCCA), which as noted above was delayed with the change of government. However the new government has indicated a commitment to the OCCA, hence we are confident that the legislation eventually will be passed.

In conjunction with OCTRF, the Ministry of Health and a community liaison committee, we assisted in the groundwork needed to develop the Ontario Breast Screening Centre, which will be affiliated with OCI/PMH. The OCI/PMH is responsible for a large region, which encompasses the City of Toronto, East York, City of York, Etobicoke, Halton Region and Peel Region. The Medical Co-ordinator, Dr. Judith Weinroth, has been appointed with support staff. The first OCI/PMH centre at 110 Bloor Street West is expected to open in the summer of 1991.

In keeping with the strategic plan developed in 1990 by Dr. R. Buick, the research areas have been restructured into five divisions, each headed by a senior scientist: Epidemiology and Statistics (N. Boyd), Cell/Molecular Biology (E.A. McCulloch), Molecular and Structural Biology (V. Ling), Experimental Therapeutics (G. Whitmore), Clinical Physics (acting head, G. Whitmore). At the end of 1990, the imaging team moved to the newly completed research institute at Sunnybrook Health Science Centre. With the planned move of this group, initiatives were undertaken in early 1990 to begin expansion of some of the biological research programs. A $750,000 grant from the Terry Fox Foundation will allow exciting new development of the structural biology team under Dr. Ling. We received this news within days of the announcement that Dr. Ling had won a Gairdner Foundation Award.

A sad note in the past year was the death of Dr. Raymond Bush. He made tremendous contributions to the field of radiation oncology during his lifetime and will greatly missed by his patients and colleagues. His colleagues have established a Visiting Professorship in his memory.

One of the issues Dr. Bush worked hard for during his tenure as Director, was a University of Toronto academic department of radiation oncology. We are pleased that this position has been approved by the University of Toronto and will be sited at Princess Margaret Hospital.

To complement that position, Dr. Gerry Goldenberg has been appointed to the newly created position of Assistant Dean of Oncology in the University of Toronto Academic Division of Oncology. Dr. Goldenberg also has based his practice at OCI/PMH.

Other new staff, appointments and retirements during the year included: Dr. Daniel Bergsagel retired in 1990 after an accomplished career and was recognized with the Order of Canada; Dr. Ian Tannock was appointed Chief of Medicine to replace Dr. Bergsagel; Dr. William Duncan returned to Scotland following completion of his five-year contract and Dr. Tom Keane was appointed Acting Head of Radiation Oncology; Dr. Ralph Blend was appointed acting head of Diagnostic Imaging to replace Dr. Steve Herman, who married and moved to Roswell Park Memorial Institute in Buffalo; Ms. Johanne Ratz, who had been with OCI/PMH since it opened, retired as Vice-President Planning; and Ms. Janet Beed from the Hospital for Sick Children was appointed as the new Vice-President of Patient Care.

In 1990 we were shocked by the sudden death of Mr. Morris Gross, a dedicated and astute member of the Board at both OCI/PMH and Mount Sinai Hospital. Earlier in the year we welcomed Ms. Laura Legge to the Board from Women's College Hospital and were pleased when Mr. Ed King, Chairman of Wood Gundy, joined the hospital as Chairman of the Princess Margaret Hospital Council.

During the 1980s, hospitals everywhere worked hard to implement quality assurance in all aspects of their organization. However, as we move into the 1990s, we realize that it is not enough to "ensure" quality, we must strive continuously to improve quality not just in patient care and research but in all support services and administration as well. The program initiative at OCI/PMH for "continuous quality improvement" will seek to ensure that the commitment to improvement evident in new methods of treating patients, is an integral part of all our operations.

D.R. Carlow, M.D.
President and
Chief Executive Officer

SPECIAL SERVICES

PROVISION OF SPECIAL DRUGS TO TREAT MALIGNANT DISEASE

The Foundation provides special chemotherapeutic agents to cancer patients who are residents of Ontario and are at home under the care of their doctors. This program was undertaken to assist those patients who find the cost of prolonged therapy with expensive drugs beyond their financial resources.

Drugs can be supplied only if attending doctors complete special prescription forms which are available from the Head Office, any of the Regional Cancer Centres, or the Princess Margaret Hospital. The completed form is mailed to the nearest Foundation centre or the Princess Margaret Hospital and the medication is mailed to the patient. The list of medications provided through the Foundation is available on request.

The total cost of the drug service during the fiscal year April 1, 1989 to March 31, 1990 was $1,005,064.94. During this period 9158 prescriptions were filled at a cost of approximately $110 per prescription.

TABLE I

Cost of Drug Service
1980–1989/90*

Year	Payments for Drugs	Total Cost
1980	259,973.32	265,059.36
1981	307,376.30	307,676.97
1982	370,388.28	375,971.20
1983	448,401.93	450,872.94
1984	569,966.52	572,300.25
1985	658,111.38	662,563.20
1986	756,111.56	760,011.54
1987	791,115.85	801,273.70
1988/89*	1,005,064.94	1,010,543.15
1989/90*	1,003,269.20	1,005,318.81

*Fiscal Year

CARCINOEMBRYONIC ANTIGEN (CEA) AND STEROID-RECEPTOR ASSAYS PROGRAM

The Ontario Cancer Treatment and Research Foundation is administering and monitoring a program for carcinoembryonic antigen (CEA) and steroid-receptor assays which is funded by the Ministry of Health. The CEA assays for confirmed cases of cancer and the steroid-receptor assays for confirmed cases of breast carcinoma are available, at no charge, to a patient when these assays are performed in the designated laboratories listed below.

Current scientific literature indicates that CEA determinations are useful primarily in patients with cancers arising from the large bowel, breast, or lung. The analytical materials available at present have little utility for tumors of other organs. The only exceptions are cancer of the cervix and medullary cancers of the thyroid.

During the fiscal period April 1, 1989 to March 31, 1990, 5322 steroid-receptor assays and 55,388 CEA assays have been performed in the designated laboratories.

All laboratories in Ontario are familiar with the program and can provide the details of the data required, sample requirements and specimen transportation. Specimens can be referred to the participating laboratories listed below either directly or through the laboratory which usually provides such services.

Laboratories in the CEA-Assay Program

McMaster University Medical Centre — Dr. E.D. Ryan
1200 Main Street West
Hamilton, Ontario L8S 4J9
tel: (416)521-2100 ext. 6293

Kingston General Hospital — Dr. M. Raymond
Stuart Street
Kingston, Ontario K7L 2V7
tel: (613)548-3232 ext. 4185

Victoria Hospital — Dr. E.R. Tustanoff
375 South Street
London, Ontario N6A 4G5
tel: (519)432-5241

Ottawa Civic Hospital 1053 Carling Avenue Ottawa, Ontario K1Y 4E9 tel: (613)725-4431	Dr. C. Lapkoff
General Hospital of Port Arthur 460 North Court Street Thunder Bay, Ontario P7A 4X6 tel: (807)343-6707	Dr. N. Escott
Sunnybrook Medical Centre 2075 Bayview Avenue Toronto, Ontario M4N 3M5 tel: (416)480-4648	Dr. A. Malkin

Laboratories in the Steroid-Receptor-Assay Program

McMaster University Medical Centre 1200 Main Street West Hamilton, Ontario L8S 4J9 tel: (416)521-2100 ext. 6293	Dr. E.D. Ryan
Victoria Hospital 375 South Street London, Ontario N6A 4G5 tel: (519)432-5241	Dr. E.R. Tustanoff
Ottawa Civic Hospital 1053 Carling Avenue Ottawa, Ontario K1Y 4E9 tel: (613)725-4420	Dr. T. Ooi
Sunnybrook Medical Centre 2075 Bayview Avenue Toronto, Ontario M4N 3M5 tel: (416)487-2722	Dr. D.J.A. Sutherland
University of Toronto Medical Sciences Bldg., Rm. 7336 Toronto, Ontario M5S 1A8 tel: (416)978-3553	Dr. G.E. Mobbs

DIAGNOSTIC BIOPSY SERVICE AND VOLUNTARY REPORTING BY PATHOLOGISTS

The number of pathology reports voluntarily submitted to the Foundation by the directors of pathology departments remained approximately 70,000 reports in 1989. These reports are used in the generation of cancer incidence data for Ontario and are most valuable in confirming the diagnosis of new cases. Under The Cancer Act of Ontario, protection is provided for physicians, dentists and hospitals reporting information on cancer cases to the Foundation. The information from the reports is only used for compiling statistics and for carrying out medical and epidemiological research.

The Foundation gratefully acknowledges the continuing co-operation of the participating pathologists and hospitals, and the support of the Ontario Association of Pathologists in the acquisition of these data.

The diagnostic biopsy service pays for biopsies on uninsured patients. In 1989, 6868 specimens were submitted by dentists (6478 in 1988).

LODGES FOR AMBULATORY CANCER PATIENTS

At present, the Foundation funds and administers seven lodges for out-of-town ambulatory cancer patients attending the regional cancer centres for diagnosis and treatment. These lodges provide comfortable, supportive accommodation, with minimal supervision, at no cost to the patient. When beds are available, escorts are accommodated at minimal cost.

The Foundation provides this accommodation because the patient often has to travel a considerable distance to reach treatment centres. Without these facilities, the patient would be admitted to hospital at far greater expense to the Province.

Shown below is a list of current facilities and number of beds:

		Number of Beds
HAMILTON	Lakeview Lodge	16
KINGSTON	Quinte-Thousand Islands Lodge	32
LONDON	Thameswood Lodge	48
OTTAWA	Maurice J. Grimes Lodge	48
	Pavillon Alta Vista Lodge	26
SUDBURY	Under construction*	70
THUNDER BAY	Amethyst House Lodge	18
TORONTO	Princess Margaret Hospital Lodge	85

Patients who require hostel accommodation while being treated at the Toronto-Bayview Regional Cancer Centre are housed in the Princess Margaret Hospital Lodge.

*To be completed in April 1991.

TRANSPORTATION OF CANCER PATIENTS

The Foundation covers the cost of transportation to any one of its regional cancer centres or to the Princess Margaret Hospital of those patients who live more than 25 miles from the centre and are considered to be in financial need. For patients 18 years or less, transportation is provided to the principal pediatric oncology treatment centres in the five health science complexes, namely:

HAMILTON	McMaster Medical Centre
KINGSTON	Kingston General and Hotel Dieu Hospitals
LONDON	War Memorial Children's Hospital, Victoria Hospital Corporation
OTTAWA	Children's Hospital of Eastern Ontario
TORONTO	Hospital for Sick Children

Usually transportation is arranged by the local unit of the Canadian Cancer Society, which subsequently is reimbursed by the Foundation.

For the fiscal year ended March 31, 1990, the total cost for transportation of patients was $912,045, compared to $826,549 for the fiscal year ended March 31, 1989.

CANCER INFORMATION SERVICE

In 1988, the Cancer Information Service, funded jointly by the Ontario Cancer Treatment and Research Foundation and the Canadian Cancer Society Ontario Division, is its fourth year of service to the citizens of Ontario.

The Service provides callers with up-to-date information on cancer and cancer-related issues. The depth of information varies from patient education material to the latest research articles. The Physician Data Query (PDQ) computerized database from the National Cancer Institute provides information on standardized methods of treatment and current clinical trials in 17 English-speaking countries throughout the world.

Utilization of the Service has increased from 3132 calls in 1987 to 7408 calls in 1990.

The demographic base remains constant. The largest group of callers are patients, family members and friends; 20% of inquiries are from patients and 40% are from family members and friends. Females continue to outnumber male callers 4 to 1.

The 1-800-263-6750 telephone number operates Monday to Friday, between the hours 9:00 and 17:00.

ONTARIO BREAST SCREENING PROGRAM

Since the announcement of its acceptance in May 1989, the staff of the Ontario Breast Screening Program (OBSP) has made steady progress towards the implementation of a province-wide service. In London, on November 9, 1990, the first of a potential 36 centres had its official opening, although it had been operating since July 1990. The Scarborough Centre opened on December 11, 1990. Centres in Hamilton, Kingston, North York, Ottawa, Sudbury, Thunder Bay, Toronto and Windsor all are advancing toward a first- or second-quarter 1991 opening. Working with corporate office and regional cancer centre personnel, administrative co-ordinators in the regions have facilitated the planning, development and implementation of these centres. As each physical facility nears completion, we have hired operational staff including secretaries, nurse examiners and registered technologists.

A program, which is sensitive to women's needs, must incorporate health-promoting behaviours, the means for close collaboration with community groups, frequent consultation with professional groups and ease of accessibility to the target population. Such an innovation has tremendous potential when it incorporates effective health-promotion strategies while offering to reduce mortality of breast cancer—the leading cause of premature death in women 50 to 69 years of age. It is the role of the provincial health promotion co-ordinator and the regional health promotion officers to facilitate this process. By the end of the first quarter of 1991, all nine regional health promotion officers will have been hired. These staff members initiate community involvement and awareness through ongoing development of materials, resources and personnel. The physician information packages and program information brochures, developed to date, have been well received. Projects targeted for completion in early 1991 include a poster, videos, and multicultural information. The regional cancer centres are extremely supportive and recognize the need for efficient planning to ensure that the program reaches the target population—women 50 to 69 years. All OBSP staff intend that these programs will be universally accessible and will ensure that individual communities play an active role in their planning and implementation.

The program has solicited community support through joint community coalitions, which play an essential role in advising the program on local community issues regarding the implementation and ongoing development of the OBSP. The global impact of the health promotion component of the program is addressed through the provincial coalition. Crucial to the successful implementation of the program, is an ongoing collaboration with such professional organizations as the Ontario Medical Association and the College of Family Physicians.

Regional medical co-ordinators play a pivotal role in addressing local issues with physicians regarding both operational and clinical issues such as changes in patterns of practice, benefits of screening and assessment, and follow-up of abnormalities. A radiology advisory committee with provincial representation from the radiology community advises the program staff on policy-related radiological issues.

The program's principal objective is a 40% reduction in mortality from breast cancer in the Province of Ontario in the next decade.

This innovative program also provides the opportunity to compile information regarding program accessibility and access by both consumers and health-care providers and to measure the effectiveness of recruitment, educational, operational and follow-up techniques.

All program components will be monitored through a plan that examines process, outcome and economic variables; this is facilitated through a computer-based, data-collection process.

An advisory evaluation committee advises the program on methods of evaluation. The staff of the OCTRF Information Systems have worked with an advisory computer group comprised of users to define the program's "software and hardware" needs from both a regional and central perspective. This collaborative approach has facilitated the design of a user-defined, client-management system.

Clearly, this province-wide initiative is based on an innovative model, which hopes to reap the benefits of community-based, health-promotion/prevention initiatives. The program will have the added benefit of reducing, significantly, mortality from breast cancer.

RESEARCH PROGRAMS

SUMMARY OF OCTRF RESEARCH

There are three programs funded through the research budget of the Foundation: one, Career Investigators; two, Research Unit, Division of Epidemiology and Statistics; and three, the Ontario Clinical Oncology Group. In addition there is laboratory and clinical research carried out by medical and radiation oncologists and by physicists all of whose salaries come from the service budget of the Foundation. Finally, much of the operating support for all of the Foundation's research is peer reviewed and comes from external granting agencies, e.g., National Cancer Institute of Canada, Medical Research Council of Canada, and Ontario Ministry of Health; this support totalled over 5 million dollars in 1990.

The following is a brief description of the three programs funded through the Foundation's research budget.

Career Investigators (Career Scientists, Research Associates, Research Scholars and Clinician Scientists)

During 1990, the Foundation provided salary and core support for 11 career scientists: Dr. G. Singh in Hamilton; Drs. S.P.C Cole,J. Gerlach and J.C. Kennedy in Kingston; Drs. A. Chambers, J.Harris, W.R. Inch and J. Koropatnick in London; and Drs. H.C. Birnboim, R.G. Hawley and R.G. Liteplo in Ottawa; 3 research associates at the University of Toronto: Drs. B.L. Gallie, H.F. Haberman and G.E. Mobbs; and 1 research scholar: Dr. G.L. Hammond in London. The Foundation also provided core grants to cover such items as secretarial support for six clinician scientists: Drs. H. Hirte (Hamilton), B. Campling (Kingston), D. Logan (Ottawa), N. Berinstein and N. Lassam (Toronto-Bayview), and A.D. Ho (Sudbury).

Research Unit, Division of Epidemiology and Statistics

The Foundation provides infrastructure support for the Research Unit of the Division of Epidemiology and Statistics. Members of the Division, which has been affiliated with the Department of Preventive Medicine and Biostatistics at the University of Toronto since 1978, compete for research operating funds through the various external granting agencies. In addition to their individual research pursuits, they assist research workers throughout the Province by providing epidemiological and biostatistical information, by responding to requests from the Ministry of Health on relevant issues, and by providing information to the scientific community and general public.

The Ontario Clinical Oncology Group (OCOG)

OCOG's objectives are to develop a clinical trials network among Ontario cancer centres and to serve as a methodologic resource for investigators interested in cancer clinical research in Ontario. Since 1982, over 2000 patients have been enrolled in a variety of multicentre clinical trials.

In the Stage I Breast Cancer Study, women with node-negative breast cancer, who had undergone lumpectomy, were randomized to local breast radiation or no further therapy. In May 1990, Dr. Roy Clark presented the results of this study to the American Society of Clinical Oncology meeting in Washington, D.C.

The Concerned Smoker Study completed recruitment of 150 subjects. In this trial, smokers with abnormal sputum cytology were randomized to the Vitamin A analogue, etretinate, or a placebo. In August 1990, Dr. A. Arnold presented the results of this study at the International UICC meetings in Hamburg.

The multicentre Phase II study, which has undertaken to determine an "acceptable" intensive combination regimen of cyclophosphamide, epirubicin and 5-fluorouracil (5FU) in patients with Stage II breast cancer, has completed recruitment. This regimen is now being compared to a standard CMF (cyclophosphamide, methotrexate and 5FU) regimen in a national clinical trial conducted by the NCIC Clinical Trials Group.

The randomized trial to evaluate the value of infusional 5FU in head and neck cancer patients receiving radiation continues to recruit patients at two centres. Over 150 patients have been randomized to either 5FU or placebo.

The randomized clinical trial to evaluate the efficacy of low-dose warfarin in the prevention of thrombosis in Stage IV breast cancer patients, continues recruitment. The trial is on target; 180 women have been entered.

The Brain Metastases Study continues recruitment. Cancer patients with a single brain metastasis are randomized to surgical removal of the metastasis plus radiation or radiation alone. Thirty-eight patients have been recruited at four centres.

In February 1990, OCOG held their annual three-day methodology workshop. At this event, 20 oncologists from across the province received "hands-on" experience in the development of a clinical protocol.

During the past year, Drs. P. McCulloch and M. Levine visited each of the Ontario cancer centres to discuss OCOG's objectives and future. These site visits proved useful in planning for OCOG's future. Each Ontario cancer centre has appointed an OCOG site representative to further improve communication and networking, and to generate ideas for future studies. The OCOG site representatives committee has already met.

Senior Scientific Staff at the Ontario Cancer Institute

In addition to the funding of the three programs just described, the Foundation is the conduit through which the provincial government provides salary and core support for the senior scientific staff at the Ontario Cancer Institute. The annual research report of the Ontario Cancer Institute describes the projects carried out by these scientists.

J.C. Laidlaw, M.D.

RESEARCH PERSONNEL SUPPORTED BY OCTRF

Career Scientists

Hamilton Regional Cancer Centre:
G. Singh, Ph.D.

Kingston Regional Cancer Centre:
S.P.C. Cole, Ph.D.
J.H. Gerlach, Ph.D.
J.C. Kennedy, M.D.

London Regional Cancer Centre:
A.D. Chambers, Ph.D.
J. Harris, Ph.D.
W.R. Inch, Ph.D.
D.J. Koropatnick, Ph.D.

Ottawa Regional Cancer Centre:
H.C. Birnboim, M.D.
R.G. Hawley, Ph.D.
R.G. Liteplo, Ph.D.

Clinician Scientists:

Hamilton Regional Cancer Centre:
H. Hirte, M.D.

Kingston Regional Cancer Centre:
B. Campling, Ph.D.

Ottawa Regional Cancer Centre:
D. Logan, M.D.

Northeastern Ontario Regional Cancer Centre:
A.D. Ho, M.D.

Toronto-Bayview Regional Cancer Centre:
N. Berinstein, M.D.
H. Lassam, M.D.

Research Associates

Toronto Western Hospital:
H.F. Haberman, M.D.

University of Toronto:
B.L. Gallie, M.D.
G.E. Mobbs, M.D.

Research Scholars:

University of Western Ontario:
G.L. Hammond, M.D.

Clinical Psychologist:

Thunder Bay Regional Cancer Centre:
S. Sellick, Ph.D.

REPORTS ON RESEARCH PROJECTS

HAMILTON

Hamilton Regional Cancer Centre:

Mitochondrial DNA (mtDNA) as a Critical Target for Cisplatin-Induced Nephrotoxicity
G. Singh 205

Chemotactic and Growth-Factor Activity of Bone-Derived TGF-beta for Bone-Metastasizing Rat Walker-256 Carcinosarcoma Cells
G. Singh and F.W. Orr 207

Immunobiology of Ovarian Carcinoma
H.W. Hirte and D.A. Clark 208

Additional Investigations 209

KINGSTON

Kingston Regional Cancer Centre:

Photodynamic Therapy for Cancer
J.C. Kennedy 211

Drug Resistance in Small Cell Lung Cancer (SCLC)
S.P.C. Cole 212

Molecular Basis of Drug Resistance in a Lung Carcinoma Cell Line
S.P.C. Cole and R.G. Deeley 213

Clinical Application of the MTT Assay
B.G. Campling and Y-M Lam 214

Clinical Drug Resistance in Small Cell Lung Cancer
B.G. Campling 216

LONDON

London Regional Cancer Centre:

Use of Magnetic Resonance Spectroscopy (MRS) to Monitor Cardiotoxicity Caused by Adriamycin and Protection by ICRF-187
W.R. Inch, S.E. Daly, E.R. Tustanoff and T.T. Thompson 218

Metallothionein Expression and Resistance to Radiation and Chemotherapeutic Drug Treatment
J. Koropatnick and M.G. Cherian 220

Somatic Cell Genetic Analysis of Metastatic Cells
J.F. Harris and A.F. Chambers 222

The Contribution of Oncogenes to Tumor Metastasis
A.F. Chambers 224

Development and Characterization of Monoclonal Antibodies to Metastatic Tumor Cells
J.F. Harris 226

Structure, Function and Hormonal Regulation of Plasma Steroid Binding Proteins
G.L. Hammond 228

Additional Investigations 231

OTTAWA

Ottawa Regional Cancer Centre:

Mechanism of Oxygen-Radical Induced Damage to Cellular DNA and its Role in Tumor Progression
H.C. Birnboim 234

In Vivo and _In Vitro_ Induction by Granulocyte-Derived Oxyradicals of Mutants at the HPRT Locus in Mouse Cells
H.C. Birnboim 237

The Involvement of Intracellular Protein Trafficking in Oncogenesis and Tumor Progression
R.G. Liteplo 239

Cytokine Network in Leukemia
R.G. Hawley 241

Identification of New Genes with a Viral Oncogene Probe
R.G. Hawley 242

Kaposi's Sarcoma - an _In Vitro_ Study
D.M. Logan, C.A. Izaguirre, L. Huebsch and C-Y. Kang 243

Determination of Metastatic Potential of Non-Small Cell Lung Carcinoma (NSCLC) and Correlation with Clinical Outcome
D.M. Logan, J.A. Maroun, R. Belanger, W.K. Evans and C.A. Izaguirre 245

Additional Investigations 247

SUDBURY

Northeastern Ontario Regional Cancer Centre:

Clinical Investigations 261

THUNDER BAY

Thunder Bay Regional Cancer Centre

Clinical Investigations 264

TORONTO

Toronto-Bayview Regional Cancer Centre:

Clinical Investigations 267

Division of Epidemiology and Statistics:

Epidemiology Research Unit
E.A. Clarke, G. Darlington, E. Holowaty, N. Kreiger
L.D. Marrett and J. McLaughlin 273

Additional Investigations 275

University of Toronto:

The Retinoblastoma (RB) Gene in Human Cancer
B.L. Gallie 283

Relationships of Pheomelanins and Photosensitizers
H.F Haberman and I.A. Menon 285

Hormone Receptor Mechanisms in the Development and Treatment of Prostatic Neoplasia
G.E. Mobbs 286

Hamilton Regional Cancer Centre

MITOCHONDRIAL DNA (mtDNA) AS A CRITICAL TARGET FOR CISPLATIN-INDUCED NEPHROTOXICITY*

G. SINGH**, *Hamilton, Ontario*

Cisplatin, a relatively new antitumor agent, is associated with renal-function impairment, the mechanisms of which are not well understood. This study used a mouse model to examine the nephrotoxicity induced by cisplatin. Both morphological and biochemical evidence suggests that the principal avenue of cisplatin-induced cellular toxicity may be mitochondrial damage. Morphological and biochemical changes are evident 72 hr after a single, 10 mg/kg (intraperitoneal) dose of cisplatin. During *in vitro* incubation of cisplatin with renal epithelial cells, we also noted a decline in Rhodamine-123 fluorescence with time, which indicated mitonchondrial damage. These findings suggest that the nephrotoxic effects of cisplatin may be related to mitochondrial damage.

Current evidence suggests that DNA is the principal intracellular target of cisplatin. Since a cell contains two distinct genomes, namely mitochondrial and nuclear, we postulate that the mtDNA is the major target for cisplatin because: (a) mtDNA is less closely associated with protein than nuclear DNA and, hypothetically, would be more accessible to attack by aquated species of cisplatin; (b) DNA repair mechanisms are abundant in the nucleus but sparse in mitochondria; and (c) cisplatin accumulates in higher concentration in mitochondria than in the nucleus. In addition, damage to mtDNA is lethal to the organelle.

We observed changes in mtDNA levels early in the course of treatment and with the 20 mg/kg dose of cisplatin observed differences between the liver and kidney. In the liver, on day 3, total mtDNA increased by approximately 172% of control, but, in the kidney, total mtDNA decreased to

---

[*] CS-106-4.

[**] Career Scientist, OCTRF Hamilton Regional Cancer Centre; and Associate Professor of Pathology, McMaster University, Hamilton.

63% of control. Also cisplatin had different effects on metallothionein mRNA in the liver and in the kidney. Following cisplatin, metallothionein levels increased in the liver but little or no changes were observed in the kidney. Similarly, we observed increases in total mtDNA in the liver, but a decrease in the kidney.

In summary, our data indicate that cisplatin induced organ-specific toxicity in the kidney via damage to mtDNA; the organ seems unable to compensate for damaged DNA.

This project is supported by a grant from the Medical Research Council of Canada.

CHEMOTACTIC AND GROWTH-FACTOR ACTIVITY OF BONE-DERIVED TGF-BETA FOR BONE-METASTASIZING RAT WALKER-256 CARCINOSARCOMA CELLS*

G. SINGH** and F.W. ORR†, *Hamilton, Ontario*

Bone is a preferred target organ for metastasis of the rat Walker-256 (W-256) carcinosarcoma and a major source of TGF-beta. Since TGF-beta stimulates the growth of some transformed cells and is a chemoattractant, we have postulated that TGF-beta, released from resorbing bone, can stimulate the growth and migration of the osteotropic W-256 cancer cell line. In the presence of 20 ng/ml EGF, purified platelet-derived TGF-beta produced a dose-dependent growth response in Walker-256 cells ($ED_{50} = 0.12 \pm 0.01$ ng TGF-beta/ml). Checkerboard analysis confirmed that the response depended upon a concentration gradient. The conditioned media from organ cultures of bone contained TGF-beta, detectable by NRK fibroblast colony formation. TGF-beta concentration correlated with resorption of bone organ cultures ($r=0.95$) and with the ability of these media to promote the growth or chemotaxis of W-256 cells ($r=0.98$, $p<0.01$). The growth-promoting and chemotactic activities in conditioned bone culture medium and that of the purified platelet-derived TGF-beta were inhibited after incubation with anti-TGF-beta1. We postulate that bone-derived TGF-beta may facilitate the establishment of metastatic tumors in bone.

This project is supported by a grant from the Medical Research Council of Canada.

---

*CS-106-5.

**Career Scientists, OCTRF Hamilton Regional Cancer Centre; and Associate Professor of Pathology, McMaster University, Hamilton.

†Professor of Pathology, McMaster University.

IMMUNOBIOLOGY OF OVARIAN CARCINOMA

H.W. HIRTE* and D.A. CLARK**, *Hamilton, Ontario*

Despite the optimal use of surgery, chemotherapy and radiotherapy, most patients with advanced ovarian carcinoma ultimately relapse and die of progressive intraperitoneal disease. In the past, immunologic approaches to treatment generally have been unsuccessful. Although these tumors often are infiltrated with immune effector cells, e.g. lymphocytes and monocytes, they are not usually in a state of activation which would allow them to kill the surrounding tumor cells. We are studying human ascitic ovarian carcinoma as a model to examine the interaction between tumor and host-immune response.

It has been possible to isolate, expand and activate tumor-associated lymphocytes (TAL) from the ascitic fluid (AF) of human ovarian carcinoma *in vitro*. These activated TAL were able to kill autologous tumor targets but generally also killed a broad range of other tumor targets. By the addition of selected mitogens and cytokines (anti-CD3 antibody, tumor-necrosis factor and interleukin-4), we hope to activate and expand cytotoxic T-lymphocytes with specificity for autologous tumor.

However, many tumors produce factors which can suppress the host-immune response. To determine whether the cell-free AF from ovarian carcinoma contained such factors, we have studied the generation of lymphokine-activated killer (LAK) cells in the presence of AF. All samples tested suppressed LAK generation to varying degrees in a time- and concentration-dependent manner. Acid HPLC elution of two highly suppressive samples revealed a major peak of suppressive activity eluting at approximately 25 kDa molecular weight. The suppressive activity of the peak-suppressive fraction and whole ascites was reversed by a neutralizing, anti-transforming, growth-factor-beta (TGF-beta) antibody. Our findings suggest that the major LAK-suppressive activity in AF is a TGF-beta-like factor. On-going studies will characterize further this factor and its cell of origin.

Understanding the factors that modulate the activity of TAL, may allow us to generate tumor-specific effectors and thus develop more effective therapy.

These projects are supported by grants from the National Cancer Institute of Canada and the Banting Research Foundation.

---

*Clinician Scientist, OCTRF Hamilton Regional Cancer Centre; and Assistant Professor of Medicine, McMaster University, Hamilton.

**Professor of Medicine, McMaster University.

ADDITIONAL INVESTIGATIONS

Dr. W.M. Hryniuk, Chief Executive Officer HRCC and Vice-President OCTRF, reports on the following clinical research investigations:

Clinical research continues to be as a major activity at the Hamilton Centre. Under the direction of Dr. Mark Levine, we are conducting clinical trials in a number of disease sites.

We continue to recruit for a multicentre randomized trial examining the role of infusional 5-FU as a radiosensitizer in patients with head and neck cancer receiving radical radiotherapy for cure. To date, over 150 patients have been entered. *(Investigator: G. Browman; funded by NCIC)*

A multicentre trial determining the efficacy of low-dose warfarin in the prevention of thromboembolic disease in women with advanced breast cancer continuous recruitment. Already over 160 women have been enrolled at a number of centres. *(Investigator: M. Levine; funded by NCIC)*

In the past year, we completed recruitment of 150 smokers in a randomized trial examining the role of Vitamin A analogue, etretinate, in reversing abnormal sputum cytology. The results of the study have been presented at the recent international UICC cancer meetings in Hamburg, Germany. *(Investigator: A. Andrew; funded by Ontario Ministry of Health)*

We continue to enrol patients in a multicentre trial evaluating the efficacy of surgery plus radiation compared to radiation alone in patients with a solitary brain metastases. *(Investigator: M. Rathbone; funded by NCIC)*

The Hamilton Centre is an active participant in the studies of the NCIC Clinical Trials Group. Currently, 250 patients are being followed on trials of hematological malignancy, breast cancer, gynecologic cancer, colorectal cancer and, more recently, anti-emetics and biological response modifiers.

At the local and regional levels, we are conducting clinical reseach projects in dose-intensive chemotherapy in advanced breast cancer, thromboembolic disease in the cancer patient. Over 850 patients are being followed on these studies.

Under the direction of Dr. Brian Wilson, basic research at the Centre continues to develop collaborative programs with McMaster University and the local teaching hospitals. Currently, eight McMaster University graduate students in physics and medical sciences are working in the department. In addition, the department is host to two postdoctoral fellows:

- Dr. Stefan Andersson-Engels, who joined us from the University of Lund, Sweden, as postdoctoral fellow, is working on *in vitro* and *in* *vivo* fluorescence imaging and spectroscopy, in collaboration with St. Michael's Hospital in Toronto; and

- Dr. Tom Farrell has been working as a postdoctoral fellow on biophysical and photobiological studies in experimental photodynamic therapy.

We have established a new collaborative program with McMaster University, Hamilton General Hospital and the University of Guelph on interstitial laserthermia for brain and liver tumors, using ultrasound and magnetic resonance imaging to monitor tissue effects.

Joint studies in preclinical photodynamic therapy have been established with Henry Ford Hospital in Detroit, Michigan.

The Hamilton Regional Cancer Centre and St. Joseph's Hospital in Hamilton have established a joint clinical program in photodynamic therapy (PDT), supported by Lederle-Cyanamid Canada Inc. Initial studies will be a Phase III trial of PDT in carcinoma *in situ* of the urinary bladder. Other regional clinical trials are being designed.

The following peer-reviewed grants are held by the Hamilton Centre staff members:

NAME	TITLE OF PROJECT	FUNDING AGENCY
KWOK, C.	Electron Dosimetry in Radioimmunotherapy US $143,000 per year 1989-92	NIH(US)
KWOK, C.	Electron Dosimetry in Heterogeneous Media $10,000 per year 1986-91	NSERC
KWOK, C. NEVILLE, A.	Whole Body Hyperthermia in Combination with Nitrosourea or Radioimmunotherapy in Human Malignant Melanoma Nude Mouse Xenografts $33,000 per year	NCIC
KWOK, C.	Radioimmunotherapy in Human Malignant Melanoma using Multicell Spheroids and Xenografts as Models $55,000 per year 1985-90	NCIC
WILSON, B. PATTERSON, M.	Development and Application of Light Dosimetry for Photodynamic Therapy $87,000 per year (1982-) 1990-93	NCIC
WILSON, B. PATTERSON, M. WYMAN, D.	Medical Laser Applications $183,000 in 1990 $215,000 per year 1991, 1992	Ontario Laser and Lightwave Research Centre of Excellence

Kingston Regional Cancer Centre

PHOTODYNAMIC THERAPY FOR CANCER*

J.C. KENNEDY**, *Kingston, Ontario*

Our research in 1990 had two main foci. In collaboration with Dr. D. Pross (Department of Oncology, Queen's University) and Dr. R.H. Pottier (Department of Chemistry and Chemical Engineering, Royal Military College), we have been developing and clinically evaluating a unique form of photodynamic therapy. By the topical application or systemic administration of the protoporphyrin precursor, 5-aminolevulinic acid (ALA), this technique induces the biosynthesis of photosensitizing concentration of protoporphyrin IX (PpIX) within the mitochondria of target cells. To date, the clinical data indicate that topical application can lead to apparently complete and long-term response in a high percentage of superficial basal cell carinomas and squamous cell carcinomas-in-situ, normally with excellent cosmetic results; however this technique is much less effective against nodular basal-cell or squamous-cell carcinomas. Topical application also has some value in the palliation of transcutaneous bleeding from nodules of carcinoma of the breast. Basic resarch, using animal models, has identified other types of normal and malignant tissues which can be photosensitized by the topical and/or systemic administration of ALA. In this respect, the endometrium and urothelium are of particular interest as targets.

In collaboration with Drs. M. Ringuet and C. Chapados (departement de chimie-biologie, Universite du Quebec a Trois Rivieres), we synthesized and partially characterized seven new photosensitizers, all of which show a strong affinity for necrotic and/or hypoxic tissues in tumors, rapid clearance from most non-malignant tissues, and low systemic (dark) toxicity. Detailed physical, chemical, and animal studies are in progress.

These projects were supported by grants from the National Cancer Institute of Canada, the Department of National Defence, and the Physicians' Services Incorporated Foundation.

---

*CS-101.

**Career Scientist, OCTRF Kingston Regional Cancer Centre; Associate Professor of Oncology and Pathology, Queen's University; and Adjunct Associate Professor of Chemistry, and Chemical Engineering, Royal Military College, Kingston.

DRUG RESISTANCE IN SMALL CELL LUNG CANCER (SCLC)*

S.P.C. COLE**, *Kingston, Ontario*

Initially, up to 90% of patients with SCLC respond to chemotherapy but almost all relapse and their long-term survival is only 5-10%. The major reason for the failure of chemotherapy is the proliferation of multidrug-resistant tumor cells. To study this problem in the laboratory, we have derived three multidrug-resistant SCLC cell lines, designated H69AR, H209/V6 and MAR/V6. Each of these displays a unique resistance phenotype. Our aim is to investigate the biology, pharmacology and immunology of non-P-glycoprotein-mediated, multidrug resistance in SCLC, using these three cell lines as model systems. One of our objectives is to identify possible biochemical mechanisms of resistance. These studies may facilitate the development of novel strategies for overcoming drug resistance in SCLC. A second objective is to examine different approaches to circumventing resistance; in this connection we are investigating the ability of alterations in growth conditions and various pharmacological agents to enhance the drug sensitivity of the three resistant SCLC cell lines. Finally, we are examining the immunological properties of these drug-resistant cells, and exploring the possibility that drug resistance may be associated with phenotypic changes, which alter recognition by the immune system. These studies may help in the rational design of new chemotherapeutic strategies which incorporate biological-response modifiers. Also they should increase our understanding of the biology of drug resistance in SCLC. In doing so, they may improve our management of this important clinical problem.

This project is supported by the National Cancer Institute of Canada, the Ontario Thoracic Society, and the Clare Nelson Bequest of the Kingston General Hospital.

---

*CS-107-2.

**Career Scientist, OCTRF Kingston Regional Cancer Centre; and Associate Professor of Oncology, and Pharmacology and Toxicology, Queen's University, Kingston.

MOLECULAR BASIS OF DRUG RESISTANCE IN A LUNG CARCINOMA CELL LINE*

S.P.C. COLE** and R.G. DEELEY†, *Kingston, Ontario*

Initially small cell lung carcinoma (SCLC) often is highly responsive to chemotherapy. However, almost invariably the disease recurs and, in the vast majority of patients, multidrug resistance (MDR) develops. In a number of different malignancies, but infrequently in SCLC, several groups of investigators have detected overexpression of P-glycoprotein, a plasma membrane protein that functions as an efflux pump to reduce drug accumulation in the cell. This raises the possibility that, in SCLC, MDR develops by a non-P-glycoprotein-mediated mechanism(s). We have isolated, and partially characterized at the biochemical level, a stable human MDR SCLC cell line, designated H69AR, in which we cannot detect overexpression of P-glycoprotein. Also we have developed monoclonal antibodies (MAbs), which recognize antigens present in H69AR cells but not in the sensitive H69 cell line. We are using these MAbs and differential and subtractive hybridization procedures to isolate cDNA clones from mRNAs overexpressed in H69AR cells. We will determine whether overexpression of the mRNAs corresponding to these cDNA clones show a causal relationship to resistance, using short-term expression of "antisense" RNA and modified "antisense" oligonucleotides to suppress expression. In both cases, we will measure alterations in chemosensitivity by a modified MTT assay. This research represents the first steps towards identifying the proteins, and ultimately the molecular mechanisms, involved in conferring the MDR phenotype to H69AR SCLC cells, which do not overexpress P-glycoprotein.

This project is supported by the Medical Research Council of Canada.

---

*CS-107-3.

**Career Scientist, OCTRF Kingston Regional Cancer Centre; and Associate Professor of Oncology, and Pharmacology and Toxicology, Queen's University, Kingston.

†Stauffer Research Professor, Cancer Research Laboratories, Queen's University, Kingston.

CLINICAL APPLICATION OF THE MTT ASSAY*

B.G. CAMPLING** and Y-M. LAM†, *Kingston, Ontario*

The practice of oncology would benefit greatly from the ability to predict response to chemotherapeutic agents. We have adapted Mosmann's MTT test for chemosensitivity testing of human cancer cell lines and fresh human tumors. The MTT test has many potential advantages over other assays of cytotoxicity because it is fast, simple and automated, and requires no washing steps and no radioisotopes. The assay can be applied to relatively small numbers of cells, and a single cell suspension is not mandatory. We have used this assay to measure the chemosensitivity of a panel of lung-cancer cell lines, and to a variety of clinical samples including solid tumors, effusions, and human leukemic blast cells. Most of the 25 drugs we have tested to date have been active in this system.

The first part of our proposal is to improve the method further, so that it can be used routinely to test the chemosensitivity of human tumors. We seek methods of separating tumor cell from non-tumor cells in samples of solid tumors and effusions. We will examine ways of analyzing the large amounts of data generated by this test, and establishing definitions of *in vitro* sensitivity and resistance. Then we will undertake a prospective clinical trial of chemosensitivity testing in acute leukemia.

We will use mathematical and statistical techniques, known collectively as response surface methodology (RSM),to examine interactions between chemotherapeutic agents. In addition, these methods will be used to examine the effects of a variety of non-chemotherapeutic agents which are reported to enhance sensitivity to chemotherapy. With multivariate statistical technique, cluster analysis, we will examine patterns of drug sensitivity and resistance in human tumor cell lines and in clinical samples. This method also will be used to examine relationships between the chemotherapeutic agents tested.

The technical advantages of the MTT assay, and the improved methods for data analysis, may overcome the limitations of other assays of drug sensitivity which have prevented their application in clinical practice. The proposed experiments may improve upon the current practice of clinical empiricism in the selection of chemotherapeutic agents, and hence improve response rates to chemotherapy.

---

*CLS-002.

**Clinician Scientist, OCTRF Kingston Regional Cancer Centre; and Assistant Professor of Oncology and Medicine, Queen's University, Kingston.

†Assistant Professor of Community Health and Epidemiology, Queen's University, Kingston.

This project is supported by a grant from the Medical Research Council of Canada

CLINICAL DRUG RESISTANCE IN SMALL CELL LUNG CANCER*

B.G. CAMPLING**, *Kingston, Ontario*

Lung cancer is the major cause of cancer-related death in North America; small cell lung cancer (SCLC) comprising 20-25% of these deaths. Combination chemotherapy is the primary treatment in SCLC, and the major reason for treatment failure is the development of resistance to chemotherapy. In many *in vitro* and *in vivo* settings, the development of resistance to multiple chemotherapeutic agents is related to the overexpression of a unique membrane protein, P-glycoprotein (P-gp). However, there is now substantial evidence that P-gp is not a frequent occurrence in multidrug resistant SCLC.

Two hypotheses have been advanced to explain the infrequent expression of P-gp in multidrug resistant SCLC: 1) The assays used to detect P-gp have not been sensitive enough to detect levels of expression that may be clinically significant; and 2) Other mechanisms of multidrug resistance may be relatively more important in this form of cancer.

Two approaches will be taken to investigate the first hypothesis. Firstly, in collaboration with Dr. J. Gerlach, an extremely sensitive molecular technique, using the polymerase chain reaction, will be employed to detect P-gp expression in a panel of SCLC cell lines. Secondly, a highly sensitive immunohistochemical technique, developed by Dr. H.S.L. Chan, will be used to detect P-gp expression in these SCLC cell lines.

Two approaches will be taken to investigate the second hypothesis. Firstly, we will examine our cell lines for reactivity with monoclonal antibodies, developed in Dr. S.P.C. Cole's laboratory; this will detect multidrug resistance associated antigens unrelated to P-gp. Secondly, we will investigate the role of glutathione and glutathione-related enzymes in our SCLC lines.

Once the methods are well established using SCLC cell lines, the results will be compared to the original tissue samples from which the cell lines were established. Then we will undertake retrospective and prospective studies on clinical samples.

---

*CLS-002-1.

**Clinician Scientist, OCTRF Kingston Regional Cancer Centre; and Assistant Professor of Oncology and Medicine, Queen's University, Kingston.

The goal of these studies is to develop assays of drug sensitivity and resistance which may be of clinical utility, and will lead to a better understanding of clinically important mechanisms of resistance in SCLC. This work will lead to prospective studies correlating expression of resistance-associated markers with response to chemotherapy, and to rationally designed clinical trials of resistance modifiers in drug-resistant tumors.

This project is funded by the Medical Research Council of Canada.

London Regional Cancer Centre

USE OF MAGNETIC RESONANCE SPECTROSCOPY (MRS) TO MONITOR CARDIOTOXICITY CAUSED BY ADRIAMYCIN AND PROTECTION BY ICRF-187*

W.R. INCH**, S.E. DALY†, E.R. TUSTANOFF‡
and T.T. THOMPSON††, *London, Ontario*

The therapeutic use of Adriamycin is limited by its cardiotoxic effect, which may be acute, occurring within minutes of its administration, or chronic, developing several weeks or months later[1]. The latter effect can be extremely debilitating and even cause death[2]. Topical magnetic resonance spectroscopy (MRS) allows measurement in intact tissues of a number of biochemical parameters, which otherwise are recognized only by destructive tissue analysis. Victoria Hospital has a spectrometer, which is capable of detecting proton (H-1), carbon (C-13) and phosphorus (P-31) resonance. Since the phosphorus atom is associated with molecules involved in energy production, this non-invasive technique can be applied to studies of cardiac metabolism.

We have developed an animal model (using New Zealand white rabbits) to study Adriamycin-induced cardiotoxicity. We have shown a correlation between the severity of the cardiomyopathy and the ratio of inorganic phosphorus-to-adenosine triphosphate. The 36 rabbits entered into this study will be divided into three groups: Control, Adriamycin, Adriamycin and ICRF-187 (PM)-1-2-bis(3,5-dioxopiperazin-1-yl)[3]. Group II and III will receive Adriamycin at a rate or 24 mg/kg/week intravenously; Group III also will receive 125 mg/kg/ ICRF-187 one hour before the Adriamycin. Group I, the control group, will receive an equivalent volume of saline.

---

*CS-100-1.

**Career Scientist, OCTRF London Regional Cancer Centre; and Professor of Oncology and Medical Biophysics, University of Western Ontario, London.

†Graduate Student, Department of Biochemistry, UWO.

‡Professor of Biochemistry, UWO.

††Assistant Professor of Radiology and Nuclear Medicine, UWO.

We will obtain baseline P-31 spectra of the heart and skeletal muscle before drug administration and at various times up to 10 weeks (total dose of Adriamycin 24 mg/kg). The electrocardiogram will be recorded at regular intervals. Histologic sections of the heart will be examined at intervals up to 10 weeks using representative animals from each group. Then the data will be analyzed to see if the protection afforded by ICRF-187 is reflected in the cardiac high-energy phosphates. If so, P-31 MRS could provide a non-invasive technique to monitor the degree of Adriamycin-induced cardiomyopathy.

REFERENCES

1. Dorshow JH, Locker GY, Myers CE: Doxorubicin. Toxicity: The interaction of drug and endogenous defence against free radical attack. *Clin Res* 1978; **26:** 434.
2. Villani F, Galimberti M, Monti E, *et al*: Effect of ICRF-187 pretreatment against doxorubicin-induced delayed cardiotoxicity in the rat. *Toxicol Appl Pharmacol* 1990; **102:** 292.
3. Speyer JL, Green MD, Kramer E *et al*: Protective effect of the bispiperazinedione ICRF-187 against doxorubicin-induced cardiac toxicity in women with advanced breast cancer. *N Engl J Med* 1988; **319:** 745.

METALLOTHIONEIN EXPRESSION AND RESISTANCE TO RADIATION AND CHEMOTHERAPEUTIC DRUG TREATMENT*

J. KOROPATNICK** and M.G. CHERIAN†, *London, Ontario*

A significant cause of failure of cancer therapy is the development of resistance to radiation or chemotherapy by malignant cells. Metallothioneins (MTs), a class of proteins, are associated with resistance to radiation and chemotherapeutic agents. MT may act as a sacrificial target, sparing critical cellular macromolecules from damage by reactive cytotoxic agents, and/or it may play a homeostatic role by supplying essential metals (Zn, Cu) for cellular repair processes[1]. We have isolated related, clonal, melanoma-cell populations with high and low constitutive MT expression, and produced a panel of chimeric, Chinese-hamster-ovary-cell lines, which express either human or mouse MT genes. All express a wide range of MT levels in the absence of heavy metal induction. We have observed that:

a) Elevated MT expression is associated with cellular resistance to the chemotherapeutic agent, cisplatin, but other effects of heavy-metal treatment (than MT induction) also are responsible for cisplatin and methotrexate resistance. Therefore, elevated MT expression in drug-resistant cells selected by heavy-metal treatment may be the results, rather than the cause, of the resistance[2].

b) However, there is a positive correlation between cisplatin resistance (but not radioresistance) and expression of transfected mouse and human MT genes in chimeric CHO cells in the absence of heavy-metal treatment. This observation suggests that MT expression at relatively low levels similar to those induced by heavy metals can mediate increased resistance to chemotherapeutic agents (Koropatnick and Pearson, manuscript submitted) similar to increased resistance to alkylating agents observed at high-level MT expression directed by a viral promoter[1].

Studies are under way to determine the range of drugs against which MT may mediate resistance, and to determine whether MT increases resistance by preventing cellular damage (radical scavenging), or by enhancing cellular repair (homeostasis) in chimeric CHO cells.

---

*CS-103-1.

**Career Scientist, OCTRF London Regional Cancer Centre; Associate Professor of Oncology, Assistant Professor of Microbiology and Immunology and Honorary Lecturer of Pathology, University of Western Ontario, London.

†Professor of Pathology, UWO.

This project is supported by the Medical Research Council of Canada

REFERENCES

1. Kaina B, Lohrer H, Karin M, Herrlich P: Overexpressed human metallothionein IIA gene protects Chinese hamster ovary cells from killing by alkylating agents. *Proc Natl Sci USA* 1990; **87:** 2710.
2. Koropatnick J, Pearson J: Zinc treatment, metallothionein expression, and resistance to cisplatin in mouse melanoma cells. *Somat Cell Molec Genet* 1990; **16:** 529.

SOMATIC CELL GENETIC ANALYSIS OF METASTATIC CELLS*

J.F. HARRIS** and A.F CHAMBERS†, *London, Ontario*

An important feature in the development of metastatic cells is the generation of heterogeneity. While we have measured the rates of generation of metastatic variant cells in several tumor models[1-4], little is know about the mechanisms for the generation of the observed heterogeneity in the metastatic phenotype.

We tested an epigenetic hypothesis for the generation of heterogeneity by examining the effects of the microenvironment on the frequency and rate of generation of metastatic variant cells in both parental B16F1 melanoma cells and nascent clones. The metastatic abilities of cultured B16F1 cells were tested after a period of growth in the presence or absence of a second cell population separated from each other by a transwell membrane (0.45 μ pore size). The first population is defined as the "responder" cells and the second as the "stimulator" cells. The presence of 10^5 B16F1 stimulator cells during the growth of responder B16F1 cells from ~10^4 to ~10^6 cells resulted in cells with an increased metastatic phenotype (>8-fold increase in median number of lung tumors relative to untreated B16F1 parental cells. Also the presence of stimulator cells increased the metastatic phenotype of nascent clones, which were grown to a population size of <10^6 cells, suggesting that the rate of generation of metastatic variants of the responder B16F1 clones was affected by the stimulator cells. Other cell lines, including highly metastatic B16F10 and BL6 melanoma cells and KHT35-L1 fibrosarcoma cells, were effective stimulator cells when as few as 10^4 cells were added to transwells. In additional, normal immortalized NIH 3T3 cells were effective stimulator cells only 10^5 cells/transwell. The cell density at which untreated parental B16F1 cells were harvested ($3x10^3$ to $3x10^5$ cells/cm^2) did not affect the median number of lung tumors significantly. These results suggest that factors released from both tumor and immortalized normal cells can modulate epigenetic changes in the metastatic phenotype of B16F1 melanoma cells.

This project was supported by the Medical Research Council of Canada.

---

*CS-150-2.

**Terry Fox (Ontario) Career Scientist, OCTRF London Regional Cancer Centre; Assistant Professor of Oncology and of Microbiology and Immunology, University of Western Ontario, London.

†Terry Fox (Ontario) Career Scientist, OCTRF London Regional Cancer Centre; Associate Professor of Oncology and of Microbiology and Immunology, UWO.

REFERENCES

1. Harris JF, Chambers AF, Hill RP, Ling V: Metastatic variants are generated spontaneously at a high rate in mouse KHT tumor. *Proc Natl Acad Sci USA* 1982; **79:** 5547.
2. Chambers AF, Harris JF, Ling V, Hill RP: Rapid phenotype variation in cells derived from lung metastases of KHT fibrosarcoma. *Invasion Metastasis* 1984; **4:** 225.
3. Harris JF, Chambers AF, Ling V, Hill RP: Dynamic heterogeneity: Characterization of two cell lines derived from experimental lung metastases of mouse KHT fibrosarcoma. *Invasion Metastasis* 1987; **7:** 217.
4. Harris JF, Best MW: Dynamic heterogeneity: Metastatic variants to liver are generated spontaneously in mouse embryonal carcinoma cells. *Clin Exp Metastasis* 1988; **8:** 451.

THE CONTRIBUTION OF ONCOGENES TO TUMOR METASTASIS*

A.F. CHAMBERS**, *London, Ontario*

We have shown that non-tumorigenic NIH 3T3 cells transformed with the T24 H-*ras* oncogene become tumorigenic and metastatic, and that their degree of malignancy (when tested in assays in both chick embryos and nude mice) is proportional to levels of expression of *ras* mRNA and p21 protein[1-3]. We have proposed that the metastatic ability in these cells is due to expression of *ras*-induced genes, which contribute more directly to metastasis[4]. We have identified several of these *ras*-induced genes[5-7], which include calcium-binding proteins, proteases, and potential adhesive proteins. We are examining the role of some of these proteins in tumor progression.

In contrast to the findings with NIH 3T3 cells, transfection and expression of the same *ras* oncogene, either alone or with a *myc* oncogene, consistently fails to promote progression of tumorigenic but non-metastatic murine LTA cells[8]. LTA and NIH 3T3 cells show major differences in their patterns of *ras*-induced gene expression. We are using the different responses of NIH 3T3 cells and LTA cells to oncogene expression as model systems to study mechanisms by which cells are responsive or resistant to oncogene signals.

This research is supported by grants from the National Cancer Institute of Canada, and the Cancer Research Society, Inc.

---

*CS-150-3.

**Career Scientist, OCTRF London Regional Cancer Centre; and Associate Professor of Oncology, and of Microbiology and Immunology, University of Western Ontario, London.

REFERENCES

1. Bondy GP, Wilson S, Chambers AF: Experimental metastatic ability of H-*ras*-transformed cells. *Cancer Res* 1985; **45:** 6005.
2. Hill SA, Wilson S, Chambers AF: Clonal heterogeneity, experimental metastatic ability, and p21 expression in H-*ras*-transformed NIH 3T3 cells. *JNCI* 1988; **7:** 484.
3. Chambers AF, Denhardt GH, Wilson SM: *Ras*-transformed NIH 3T3 cell lines, selected for metastatic ability in chick embryos, have increased proportions of p21-expressing cells and are metastatic in nude mice. *Invasion Metastasis* 1990; **10:** 225.
4. Chambers AF, Tuck AB: Oncogene transformation and the metastatic phenotype. *Anticancer Res* 1988; **8:** 861.
5. Craig AM, Nemir M, Mukherjee BB, Chambers AF, Denhardt DT: Identification of the major phosphoprotein secreted by many rodent cell lines as 2ar/osteopontin: Enhanced expression in H-*ras*-transformed 3T3 cells. *Biochem Biophys Res Commun* 1988; **157:** 166.
6. Guo X, Chambers AF, Parfett CLJ *et al*: Identification of a serum-inducible mRNA (5B10) as the mouse homolog of calcyclin: Tissue distribution and expression in metastatic, *ras*-transformed NIH 3T3 cells. *Cell Growth Diff* 1990; **1:** 333.
7. Craig AM, Bowden GT, Chambers AF *et al*: Secreted phosphoprotein mRNA is induced during multistage carcinogenesis in mouse skin and correlates with the metastatic potential of murine fibroblasts. *Int J Cancer* 1990; **46:** 133.
8. Tuck AB, Wilson SM, Chambers AF: *Ras* transfection and expression does not induce progression from tumorigenecity to metastatic ability in mouse LTA cells. *Clin Exp Metastasis* 1990; **8:** 471.

DEVELOPMENT AND CHARACTERIZATION OF MONOCLONAL ANTIBODIES TO METASTATIC TUMOR CELLS*

J.F. HARRIS**, *London, Ontario*

Potentially, monoclonal antibodies (MAbs) are incisive reagents for analyses of cell-surface phenotypes of metastatic cells. Since MAbs can resolve some properties of individual cells, they may be used to investigate cell heterogeneity, which we have shown to be a fundamental issue in metastasis[1-4]. We have examined the binding and functional activity of MAb SG-1, which was raised by immunization using mouse embryonal carcinoma cells and screened using KHT fibrosarcoma cells[5]. Quantitative absorption, binding and *in situ* immunochemical staining assays indicate that the MAb SG-1-defined epitopes are expressed preferentially by the highly metastatic KHT35-L1 cells relative to the weakly metastatic, parental KHTp cells. Furthermore, there was a significant correlation ($p<0.05$) between the expression of MAb SG-1-defined antigen on KHT cells and their metastatic ability.

We found that treatment of KHT35-L1 cells with MAb SG-1 at (1-10 µg/ml *in vitro* for one hour followed by washing significantly enhances the experimental metastatic phenotype. The increase in metastatic phenotype does not depend on antibody bound to the cell surface since MAb SG-1 elutes from the surface of viable cells within minutes. Treatment with MAb SG-1 does not change the kinetics of attachment and retention of injected radiolabelled tumor cells in the lung. We are examining the hypothesis that binding of MAb SG-1 to cells results in a signal transduction process, which alters the metastatic phenotype of cells containing the antigen receptor.

Initial characterization of antigen from KHT cells indicates that the epitope of MAb SG-1 is defined by sulfated glycoconjugates containing galactose and sulfate[5]. The differential expression of this antigen in KHTp and KHT35-L1 cells was detected primarily in chloroform/methanol soluble molecules. Accordingly, we have enriched the antigen from the total chloroform/methanol extracts using two-dimensional, silica-thin layer chromatography. We are developing such antigen purification strategies to define the antigen's structure by mass spectroscopy analysis.

---

*CS-151-3.

**Terry Fox (Ontario) Career Scientist, OCTRF London Regional Cancer Centre; Assistant Professor of Oncology, and of Microbiology and Immunology, University of Western Ontario, London.

This project was supported by the Medical Research Council of Canada, and the Victoria Hospital Research Development Fund.

REFERENCES

1. Harris JF, Chambers AF, Hill RP, Ling V: Metastatic variants are generated spontaneously at a high rate in mouse KHT tumor. *Proc Natl Acad Sci USA* 1982; **79:** 5547.
2. Chambers AF, Harris JF, Ling V, Hill RP: Rapid phenotype variation in cells derived from lung metastases of KHT fibrosarcoma. *Invasion Metastasis* 1984; **4:** 225.
3. Harris JF, Chambers AF, Ling V, Hill RP: Dynamic heterogeneity: Characterization of two cell lines derived from experimental lung metastases of mouse KHT fibrosarcoma. *Invasion Metastasis* 1987; **7:** 217.
4. Harris JF, Best MW: Dynamic heterogeneity: Metastatic variants to liver are generated spontaneously in mouse embryonal carcinoma cells. *Clin Exp Metastasis* 1988; **6:** 451.
5. Harris JF, Beaton DW: Sulfated glycoconjugate determinants recognized by monoclonal antibody SG-1, correlate with the experimental metastatic ability KHT firbrosarcoma cells. *Clin Exp Metastasis* 1990; **8:** 361.

STRUCTURE, FUNCTION AND HORMONAL REGULATION OF PLASMA STEROID BINDING PROTEINS*

G.L. HAMMOND**. *London, Ontario*

This year we continued our studies in the molecular biology and physiology of the extracellular steroid transport proteins: corticosteroid binding globulin (CBG) and sex hormone binding globulin (SHBG)[1]. These two high-affinity binding proteins not only transport steroids in the blood but also regulate steroid bioavailability, and may participate in the delivery of steroids to target cells[2].

To further characterize the human SHBG[3] and CBG[4] genes, we have determined their chromosomal location in collaboration with Dr. Bérubé at Laval University[5,6]. The human CBG gene is located in the same region of chromosome 14 (p12-13) as two other structurally-related serine proteinase inhibitors (SERPINs), alpha1-antitrypsin and alpha1-antichymotrypsin, while the human SHBG gene is located on the short arm of chromosome 17 (q31-q32.1) in the vicinity of the p53 tumor suppressor gene. We postulate that the relationship between CBG and other SERPINs may have some functional significance[7], and now have demonstrated that, during inflammation, the interaction between CBG and neutrophil elastase occurs on the neutrophil surface, does not involve the internalization of CBG[8], and thereby may promote the delivery of glucocorticoids to these cells during this process[9].

We have completed our studies of the ontogeny and hormonal control of CBG biosynthesis in the rat[10]. We have also discovered that the CBG gene of BB diabetic rats contains a point mutation, which results in the production of a variant CBG with an abnormal affinity for glucocorticoids. Recently, point mutations also have been identified in the human CBG genes for three genetic variants with reduced cortisol-binding affinities. The rat CBG gene also has been cloned and its promoter region is being used to identify transcription factors responsible for the gene's hormonal regulation. Since CBG is an acute-phase negative protein, we expect to identify factors involved in the down-regulation of CBG biosynthesis during inflammation. Also we have cloned and characterized a cDNA for rabbit CBG and used it to extend our studies of the developmental changes in CBG biosynthesis in the fetus[11,12]. Similarly, in collaboration with Dr. John Challis, we have obtained cDNAs for sheep CBG and, in the fetal lamb, have studied the regulation of CBG biosynthesis in the liver and other tissues.

---

* RS-230.

** OCTRF Research Scholar; Director Cancer Research Laboratories, London Regional Cancer Centre; and Professor of Obstetrics and Gynecology and Oncology, University of Western Ontario, London.

We have constructed a full-length cDNA for human SHBG and used it to obtain stable transfectants, which produce and secrete high levels of SHBG in culture medium. In terms of steroid-binding characteristics and other physicochemical properties, the SHBG produced CHO cells or a mouse-hepatoma cell line are identical to SHBG in human pregnancy serum, but there are cell-specific differences in the glycosylation of the protein. Now this construct is being modified to map the steroid-binding domain of SHBG and to assess the functional significance of carbohydrate additions. We have begun similar studies involving site-directed mutagenesis and expression of human and rat CBG cDNAs. In this way, we hope to obtain new information about the steroid-binding sites of these proteins and other structural elements which may be important physiologically.

These projects are funded by the Medical Research Council of Canada, and the Ontario Thoracic Society.

REFERENCES

1. Hammond GL: Molecular properties of corticosteroid binding globulin and the sex-steroid binding proteins. *Endocr Rev* 1990; **11:** 65.
2. Siiteri PK, Murai JT, Hammond GL, Nisker JA, Raymoure WJ, Kuhn RW: The serum transport of steroid hormones. *Recent Prog Horm Res* 1982; **38:** 457.
3. Hammond GL, Underhill DA, Rykse HM, Smith CL: The human sex hormone binding globulin gene contains exons for androgen binding protein and two other testicular messenger RNAs. *Mol Endocrinol* 1989; **3:** 1869.
4. Underhill DA, Hammond GL: Organization of the human corticosteroid binding globulin gene and analysis of its 5' flanking region. *Mol Endocrinol* 1989; **3:** 1448.
5. Seralini G-E, Bérubé D, Gagne R, Hammond GL: The human corticosteroid binding globulin gene is located on chromosome 14 q31-q32.1 in the proximity of two other serine protease inhibitor genes. *Human Genet* 1990; **86:** 73.
6. Bérubé D, Seralini G-E, Gagne R, Hammond GL: Localization of the human sex hormone-binding globulin gene (SHBG) to the short arm of chromosome 17 (17p12-p13). *Cytogenet Cell Genet* 1990; **54:** 65.
7. Hammond GL, Smith CL, Goping IS, Underhill DA, Harley MJ, Reventos J, Musto NA, Gunsalus GL, Bardin CW: Primary structure of human corticosteroid binding globulin deduced from hepatic and pulmonary cDNAs exhibits homology with serine protease inhibitors. *Proc Natl Acad Sci USA* 1987; **84:** 5153.

8. Hammond GL, Smith CL, Underhill CM, Nguyen VTT: Interaction between corticosteroid binding globulin and activated leukocytes *in vitro*. *Biochem Biophys Res Commun* 1990; **172:** 172.

9. Hammond GL, Smith CL, Paterson NAM, Sibbald WJ: A role for corticosteroid binding globulin in delivery of cortisol to activated neutrophils. *J Clin Endocrinol Metab* 1990; **71:** 34.

10. Smith CL, Hammond GL: Ontogeny of corticosteroid binding globulin biosynthesis in the rat. *Endocrinology* 1991; **128:** 983.

11. Seralini G-E, Smith CL, Hammond GL: Rabbit corticosteroid binding globulin: Primary structure and biosynthesis during pregnancy. *Mol Endocrinol* 1990; **4:** 1166.

12. Seralini G-E, Underhill CM, Smith CL, Nguyen VTT, Hammond GL: Biological half-life and transfer of maternal corticosteroid binding globulin (CBG) to amniotic fluid in the rabbit. *Endocrinology* 1989; **125:** 1321.

ADDITIONAL INVESTIGATIONS

Dr. L. Levin, Chief Executive Officer LRCC and Vice-President OCTRF, reports on the following clinical research investigations.

PORTAL IMAGING

Investigators: P. Munro, J. Battista, A. Porter and A. Fenster
We have developed a digital fluoroscopic imaging system that can radiograph the radiotherapy patient before and while undergoing external-beam treatment. The system uses a metallic-phosphor plate to detect the megavoltage radiation exiting from the patient, and a video camera to capture the images for instant viewing on a computer work station. Extensive physics studies have characterized image performance and a clinical evaluation is under way.

Preliminary results confirm that the system may be extended to brachytherapy patients, allowing verification of source positions and dwell times in high dose rate applications.

THREE-DIMENSIONAL RADIOTHERAPY PLANNING

Investigators: J. Battista, L. Santon, L. Papiez and G. Sandison
We are developing computer techniques to advance the current practice of two-dimensional radiotherapy planning. Three aspects are being studied:

a) more accurate computation of dose distributions for megavoltage photon and electron beams, using new algorithms which consider the penetration and scattering of radiation through heterogeneous tissues;
b) more interacting displays of CT data sets, beam geometrics and dose distributions on three-dimensional computer work stations; and,
c) assuring three-dimensional consistency of all image data used during treatment planning including simulator radiographs, CT scan images and also portal images.

BRACHYTHERAPY WITH NEW RADIOACTIVE SOURCES

Investigators: A.T. Porter, J. Battista and R. Barnett
In collaboration with Amersham International, we are studying the physics and radiobiology of new radiation sources for brachytherapy. We have characterized ytterbium-69, which emits photons with an average energy of 93 keV, and decays with a half-life of 30 days. This source has potential clinical advantages for both permanent and temporary implants.

It offers an intermediate energy emission, which greatly simplifies radiation protection of staff, and yet maintains enough penetration to achieve good uniformity of dose within the target volume in the patient. The half-life also has a radiobiological advantage over iodine-125 because it allows delivery of the dose at a higher initial rate.

PROSTATIC CANCER

Investigator: A. Porter

The London Regional Cancer Centre is at the forefront of clinical research in brachytherapy for prostatic cancer. In collaboration with the Division of Nuclear Medicine, Victoria Hospital, it is the national co-ordinating centre for strontium studies in prostatic cancer.

BRAIN TUMOR STUDIES

Malignant glioma in adults will continue to be the focus of our research. We are involved in clinical trials of newly diagnosed and recurrent malignant glioma (CNS Cancer Consortium; National Cancer Institute of Canada), newly diagnosed and recurrent anaplastic oligodendroglioma (National Cancer Institute of Canada), primary CNS lymphoma (Radiation Therapy Oncology Group), low-grade glioma (Brain Tumor Co-operative Group/Radiation Therapy Oncology Group/Southwest Oncology Group), and solitary brain metastasis (Ontario Clinical Oncology Group). Steroid effects on MRI-brain-tumor images, studies of cognitive function in brain tumor patients, outcome prediction, and a variety of retrospective studies are underway or planned. Our basic research interests include molecular studies of familial glioma, experimental glioma metastasis and mechanisms of radio- and chemoresistance in glial tumors.

COLORECTAL CANCER

Investigator: J. Skillings

Investigational drug trials continue in colorectal, gastric and pancreas cancers.

SARCOMA

Investigators: V. Bramwell and A. Hammond

Dr. Bramwell remains the national co-ordinator/chairperson of the Canadian Sarcoma Group (CSG). This group is running two neoadjuvant studies in soft tissue and bone sarcoma in collaboration with European groups, and an investigational new drug study (NCIC IND.55, 10-EDAM).

All these studies are conducted under the auspices of the NCIC Clinical Trials Group. Through the London Regional Cancer Centre, additional studies are being done for spindle-cell sarcomas of bone and high-dose chemotherapy, and autologous bone marrow transplantation after resection of pulmonary metastases in soft tissue sarcoma. In December 1990, the CSG held a successful Terry Fox Workshop in London, Ontario, focusing on the molecular biology of sarcomas. As a result of this meeting, this group plans to set up a national tumor tissue bank.

MELANOMA AND RENAL CANCER

Investigators: V. Bramwell and W. Mertens

These studies, which are in their third and final year, are on target for accrual. We have submitted a grant application to explore further the immunomodulatory effects of interleukin-2 in combination with other biological response modifiers.

BREAST CANCER

The breast multidisciplinary team is a leading contributor to the recently opened NCIC-MA.5 study in premenopausal Stage II breast cancer. They have registered significant accruals in other NCIC studies, such as MA.4 and IND.45 (Menogaril), and an OCOG low-dose warfarin study. Using the OCOG data set, Dr. Skillings, with other collaborators, is undertaking a prognostic factor analysis in Stage I breast cancer. Dr. Ted Vandenberg is the study chairman of the NCIC Phase II study assessing 10-EDAM (IND.60) in metastatic breast cancer. This assessment will use multivariate analysis of classical and new markers to determine prognosis in breast cancer.

Ottawa Regional Cancer Centre

MECHANISM OF OXYGEN-RADICAL INDUCED DAMAGE TO CELLULAR DNA AND ITS ROLE IN TUMOR PROGRESSION*

H.C. BIRNBOIM**, *Ottawa, Ontario*

Oxygen radicals such as superoxide anion (O_2^-) and hydrogen peroxide (H_2O_2) are generated *in vivo* from a variety of sources, the strongest of which are phagocytic cells. Granulocytes, monocytes and macrophages can liberate large amounts of O_2^- in response to a variety of particulate and soluble stimuli, including the tumor promoter, phorbol myristate acetate (PMA). A membrane-bound enzyme complex (the "respiratory burst oxidase") uses intracellular NADPH to reduce bimolecular oxygen to O_2^-, which in turn can dismute to H_2O_2. We have shown that these oxyradicals can cause DNA strand breaks in the producing "effector" cell as well as in neighbouring "target" cells. Since phagocytic cells are found frequently in solid tumors, we have postulated that the oxyradicals they produce can cause DNA breaks and chromosome breaks in early tumor cells, thereby contributing to tumor "progression" stages of cancer evolution. Assuming that early cancer cells have suffered one genetic alteration, such as activation of the H-*ras* oncogene, phagocyte-derived oxyradicals may be responsible for additional genetic changes such as activation of other oncogenes or inactivation of anti-oncogenes.

We have continued "biochemical" studies into the mechanisms by which O_2^- and H_2O_2 cause DNA strand breaks in human granulocytes. Using highly purified granulocytes, we now find that neither catalase, which removes extracellular H_2O_2, nor superoxide dismutase (SOD), which converts O_2^- to H_2O_2 and O_2, blocks strand breaks. The explanation for this observation remains uncertain since both O_2^- and H_2O_2 can be detected in large quantities outside the cell and should be eliminated, at least in part, by the added enzymes. Lipophilic synthetic SODs, such as copper– diisopropylsalicylate complex, afforded marked protection against strand breaks but recently we have demonstrated that such compounds act by damaging the respiratory burst oxidase (thereby preventing cells from making O_2^-) and not by eliminating O_2^-. Lipophilic catechol compounds such as pyrocatechol, gossypol and urushiol block breaks by O_2^- but they also protect against H_2O_2-induced breaks. Similarly, a series of lipophilic iron chelators prevent breaks by both O_2^- and H_2O_2. We believe that O_2^- and H_2O_2 do indeed act differently to produce strand breaks since we have shown that sodium fluoride and sodium orthovanadate have opposing effects on the breaks caused by the two agents. The latter results support the hypothesis that O_2^- and H_2O_2 produce breaks by at least partially different mechanisms.

---

*CS-104-2.

**Career Scientist, and Head of Experimental Oncology, OCTRF Ottawa Regional Cancer Centre; and Professor of Medicine, of Microbiology and Immunology, and of Biochemistry, University of Ottawa.

To characterize the mechanism of oxyradical-induced strand breaks further, an independent method for analyzing breaks is being developed. We intend to determine whether breaks are induced at random or at specific genomic locations and whether they are single or double-stranded. One would not expect site-specificity of strand breakage if breakage is due to intracellular generation of freely diffusing reactive species or to random distribution of transition metals attached to DNA. Specific breakpoints might occur if a more specific enzymatic mechanism is involved. In our method, granulocytes, containing breaks induced by oxyradicals are embedded in agarose beads and deproteinized. The presence of single *vs* double strand breaks will be determined using pulse field electrophoresis. The specificity of break sites will be determined by limited exposure of cells to alkali to allow unwinding around the breakpoint; then DNA in the vicinity of breakpoints will be labelled using random hexanucleotide primers. This labelled DNA will be used to probe a battery of known genes. Because these conditions of labelling are different than those usually used in preparing probes, certain difficulties were encountered. These have been overcome and the experiment is being continued.

A new model system has been developed to investigate further the possible involvement of oxyradicals in tumor progression. An activated H-*ras* oncogene was introduced into primary rat embryo fibroblasts (REF) using a retroviral vector[1] to produce a population of REF/*ras* cells. When the cells were exposed to oxyradicals generated by human granulocytes, we detected variants with more "aggressive" growth properties including the formation of large foci on plastic petri dishes, of anchorage-independent colonies growing in soft agarose, and of large spheroids growing on the surface of firm agarose layers. REF/*ras* cells alone showed low levels of the same phenotypes but primary REF cells did not. The largest increase in "aggressive" cells were seen in cells treated with PMA-stimulated granulocytes. Some clones of "aggressive" spheroids exhibited a novel phenotype: they were able to burrow through agarose layers and grow as a monolayer on the plastic surface below. Such cells apparently are able to elaborate an "agarosase" activity; fluorescent-labelled agarose has been prepared in order to further characterize this activity.

This project is supported by a grant from the Medical Research Council of Canada.

REFERENCE

1. Compere SJ, Baldacci PA, Sharpe AH, Jaenisch R: Retroviral transduction of the human c-Ha-ras-1 oncogene into midgestation mouse embryos promotes rapid epithelial hyperplasia. *Mol Cell Biol* 1989; **9**: 6.

IN VITRO AND *IN VIVO* INDUCTION BY GRANULOCYTE-DERIVED OXYRADICALS OF MUTANTS AT THE HPRT LOCUS IN MOUSE CELLS*

H.C. BIRNBOIM**, *Ottawa, Ontario*

HPRT (hypoxanthine phosphoribosyltransferase) is an X-linked gene and therefore is present as a single copy in normal male cells. Clinically, complete HPRT deficiency is associated with Lesch-Nyhan syndrome and partial deficiency with hyperuricemia and gouty arthritis. Experimentally, it is a useful gene for the study of genomic alterations such as mutations and deletions because we can distinguish between cells either lacking or containing the functional gene. Cells lacking the gene product are completely resistant to the cytotoxic effects of guanine analogues such as 6-thioguanine (TG). Conversely, cells with an active gene product are resistant to killing by aminopterin in the presence of hypoxanthine and thymidine (HAT medium). We have been attempting to establish a murine cell line which can detect with high sensitivity the induction of mutations at the HPRT locus. Once established, this cell line will be used for *in vivo* and *in vitro* experiments to determine whether phagocytic cells, such as granulocyte or macrophages, can cause mutagenic events. We will use this model to test our hypothesis that phagocytic cells in solid tumors contribute to tumor progression by generating genotoxic compounds, such as oxygen-free radicals, which cause genomic alterations.

The cell type used was a transplantable mouse fibrosarcoma tumor line. Initially it proved to be very difficult to induce HPRT mutants in this cell, using oxyradicals, ionizing radiation or chemical mutagens. We assume that inactivation of the HPRT gene caused by chromosome breaks or large deletions led to the loss of other X-linked genes essential for cell viability. Since there is only one copy of the X chromosome, this would be a lethal event. Our strategy therefore has been to inactivate the endogenous X-linked HPRT gene and introduce an exogenous HPRT gene onto an autosome, since there should be two copies of each autosome. In this way, loss of the new HPRT gene and any associated vital genes on one chromosome would not be lethal since the second copy of the autosome would be intact. With considerable difficulty, we generated a few clones of cells lacking a functional X-linked HPRT gene. Phenotypically, these clones have been very stable, that is, their reversion frequency is <1 in 10^7. We introduced a human HPRT minigene (from Dr. P. Patel) by electroporation and isolated about 10 HAT-resistant clones. However, mover of these clones were phenotypically unstable, that is, they became TG-resistant at a frequency of about 1 in 10^4 after removal from HAT medium. In a second independent experiment we recovered a higher number of HAT-resistant clones. When tested for their phenotypic stability, 5 of 30 clones appear to be promising; they show <1 in 10^5 TG-resistant revertants after growth in HAT-free medium for a few weeks. Although deriving such lines has proved to be difficult, we anticipate that recovery of a cell line with the desired characteristics will allow us to establish a useful quantitative model system for studying phenotypic and genotypic alterations induced *in vivo* and *in vitro* by oxyradicals.

---

*CS-104-3.

**Career Scientist, and Head of Experimental Oncology, OCTRF Ottawa Regional Cancer Centre; and Professor of Medicine, Microbiology and Immunology, and of Biology, University of Ottawa.

This project is supported by a grant from the National Cancer Institute of Canada.

THE INVOLVEMENT OF INTRACELLULAR PROTEIN TRAFFICKING IN ONCOGENESIS AND TUMOR PROGRESSION*

R.G. LITEPLO**, *Ottawa, Ontario*

A major focus in cancer biology involves identifying the biochemical, cellular and molecular mechanisms responsible for the autonomous growth of tumor cells, and which are associated with, or contributing to, the "malignant phenotype". Our previous studies focused upon the relationship between the altered methionine auxotrophy (requirement) and increased growth autonomy of human tumor cells. These investigations indicate that alterations in intracellular protein trafficking and processing may be intimately linked with the oncogenic process and with the "progression" of human tumors from relatively benign to highly malignant and autonomous states.

Normal cells are able to grow in culture medium devoid of exogenous methionine but containing its immediate precursor, homocysteine. In contrast, most human tumor cell lines exhibit a reduced ability to grow in such methionine-free, homocysteine-supplemented culture medium. Earlier we found that the increased growth autonomy of human melanoma and neuroepithelioma cell lines was associated with an inability to proliferate in methionine-free, homocysteine-supplemented medium. We found that this metabolic defect is due not to the lack of sufficient methionine synthetase enzyme but rather to a deficiency in the accumulation of cobalamin and it metabolites. Cobalamin is a required cofactor for the intracellular synthesis of methionine and we have found that highly growth-autonomous, human melanoma and neuroepithelioma cells accumulate reduced amounts of cobalamin and its metabolites. Cobalamin is taken up into cells by a process involving receptor-mediated endocytosis. The reduced intracellular accumulation of cobalamin is not due to its diminished uptake, but rather to its greater efflux from the highly growth-autonomous cells. Also we have found that highly growth-autonomous human melanoma and neuroepithelioma cells exhibit an altered sensitivity to monensin, a Na+/H+ ionophore that influences intracellular protein trafficking and processing. In a series of related studies, we have also observed that rodent cells transformed by the Kirsten and Moloney murine sarcoma viruses exhibit dra-

---

[*] CS-108-2.

[**] Career Scientist, OCTRF Ottawa Regional Cancer Centre; and Assistant Professor of Medicine and Biochemistry, University of Ottawa.

matically increased resistance to the cytostatic and cytotoxic actions of monensin compared to their normal counterparts. These observations suggest that alterations in the endocytic-recycling pathways of intracellular protein trafficking and processing may make a fundamental contribution to the increased growth autonomy and progression of neoplastic cells.

This project is supported by a grant from the National Cancer Institute of Canada.

CYTOKINE NETWORK IN LEUKEMIA*

R.G. HAWLEY**, *Ottawa, Ontario*

Myeloid leukemias are diseases of neoplastic hematopoietic precursors—stem cells and progenitor cells. Recently several workers have reported the autostimulatory production of interleukin (IL-)-1 and IL-6 by the transformed progenitor (blast) cells in acute myeloid leukemia (AML). In order to investigate the *in vivo* hematopoietic activities of these cytokines and to gain insight into the molecular mechanisms of stem cell regulation/dysregulation, we have developed retrovirus-mediated, gene transfer technology to introduce transcriptionally-active IL-1 and IL-6 genes into the stem cells, which reconstitute the hematopoietic systems of lethally irradiated mice. Significant progress has been made in the past year; we have demonstrated sustained expression of exogenous IL-1 and IL-6 genes in mice for periods up to 10 months following bone-marrow transplantation. Most mice exhibited alterations in hematopoiesis which, in extreme cases, was manifest as drastic elevations in peripheral leukocytes. Current studies involve serial transplantation of the "genetically-modified" stem cells into secondary recipients in order to determine whether the persistent leukocytosis might progress to leukemia.

To gain further understanding of the molecular lesions involved in neoplastic transformation, we are attempting to isolate leukemic variants of a cytokine-dependent, myelomonocytic cell line (OTT1), which we established recently from mouse bone marrow. OTT1 cells originated from a progenitor cell capable of granulocytic or monocytic differentiation and, for growth *in vitro*, remain dependent on either IL-3, IL-5, or granulocyte-macrophage, colony-stimulating factor. Like AML blast cells, OTT1 cells constitutively produce IL-1 and IL6. We expect to identify mutations in genes whose protein products are components of the cytokine-signaling pathways.

These projects are supported by grants from the National Cancer Institute of Canada and The Arthritis Society.

---

*CS-110-3.

**Career Scientist, OCTRF Ottawa Regional Cancer Centre, General Division; and Assistant Professor of Medicine, and of Microbiology and Immunology, University of Ottawa.

IDENTIFICATION OF NEW GENES WITH A VIRAL ONCOGENE PROBE*

R.G. HAWLEY**, *Ottawa, Ontario*

The v-*cbl* (pronounced sybil) oncogene of the Cas NS-1 retrovirus induces B-cell leukemias/lymphomas in mice. The human cellular homolog of v-*cbl* (i.e., c-*cbl* proto-oncogene) resides on the long arm of chromosome 11 in a region (q23) frequently rearranged in human leukemias. DNA sequence analysis of v-*cbl* has revealed significant similarity to the yeast transcription factor GCN4, suggesting that c-*cbl* may be a regulator of gene expression.

During the cloning of a complementary DNA (cDNA) of c-*cbl* from mouse testis messenger RNA (mRNA) with a v-*cbl* probe, we isolated several cDNAs of unknown provenance. DNA sequence analysis of one of these novel clones indicates that it represents a previously unrecognized gene. Besides testis, elevated mRNA levels corresponding to this gene are found in brain and spleen of adult mice; the gene is also transcribed in several mouse tumors. Although we do not know the function of this gene at present, its evolutionary conservation in species as diverse as chickens, suggest that it may play an important role in developmentS processes. Further studies directed toward the identification of the protein product of this gene will seek to determine whether mutated forms of this protein are present in the tumors in which the gene is expressed.

This project is supported by a grant from the Leukemia Research Fund.

---

*CS-110-3.

**Career Scientist, OCTRF Ottawa Regional Cancer Centre, General Division; and Assistant Professor of Medicine, and of Microbiology and Immunology, University of Ottawa.

KAPOSI'S SARCOMA — AN *IN VITRO* STUDY[*]

D.M. LOGAN[**], C.A. IZAGUIRRE[†], L. HUEBSCH[††] and
C.Y. KANG[‡], *Ottawa, Ontario*

During the course of their illness, approximately 30% of patients with acquired immunodeficiency syndrome (AIDS), particularly male homosexuals, develop epidemic Kaposi's sarcoma (EKS). Significant morbidity occurs when the pathognomonic violaceous nodules hemorrhage, ulcerate, or cause lymphedema or mechanical obstruction. Current therapies induce only temporary and partial remission[1].

In the past, it was difficult to study the biological characteristics of EKS and to design more effective therapies because we could not establish long-term cell cultures. Two or three years ago we established and since have maintained and characterized three EKS-derived cell lines from skin biopsies of three different patients[2].

Our investigations are focusing on the growth characteristics of our EKS-derived cell lines. We have determined: that our EKS-derived cell lines require fetal-calf serum, endothelial cell growth factor and heparin to maintain growth; that EKS-derived cell proliferation is enhanced virus-free supernatant from HIV-infected HUT78 T cells or EKS-derived cells; and that the HIV-regulatory protein, tat, obtained from supernatants of recombinant baculovirus infected cells stimulates the proliferation of the enhanced EKS-derived cell. In collaboration with Dr. S. Miles, UCLA AIDS Center, Los Angeles, California, we have determined that active growth factors in the EKS-derived cell supernatant is interleukin-6[3].

We are pursuing other studies to determine whether the virus-free HIV-infected HUT78 cell supernatant and the EKS-derived cell supernatant contain other biologically active growth factor(s). In addition, we hope to determine the mechanism by which tat induces proliferation of EKS-derived cells. The long-term goal of these investigations is to define the biological characteristics of EKS and to design effective therapies to reduce EKS morbidity.

---

[*] CLS-001-1.

[**] Clinician Scientist, OCTRF Ottawa Regional Cancer Centre, General Division; and Assistant Professor of Medicine, University of Ottawa.

[†] Chief, Division of Infectious Immunology, Federal Centre for AIDS, Health and Welfare Canada; and Adjunct Professor of Microbiology and Immunology, University of Ottawa.

[††] Hematologist, Ottawa General Hospital; and Assistant Professor of Medicine, University of Ottawa.

[‡] Chairman and Professor, Department of Microbiology and Immunology, University of Ottawa.

This project is supported by Health and Welfare Canada, Research and Development Program Grants.

REFERENCES

1. Odajnyk C, Muggia FM: Treatment of Kaposi's sarcoma: Overview and analysis by clinical setting. *J Clin Oncol* 1985; **3:** 1277.
2. Logan D, Kang C-Y, Izaguirre CA, Huebsch L: Kaposi's sarcoma - An in vitro study. *Clin Invest Med* 1988; **11:** 4.
3. Miles, SA, Rezai AR, Slazar-Gonzalez JG *et al*: AIDS Kaposi's sarcoma-derived cells produce and respond to interleukin-6. *Proc Natl Acad Sci (USA)* 1990; **87:** 4060.

DETERMINATION OF METASTATIC POTENTIAL OF NON-SMALL CELL LUNG CARCINOMA (NSCLC) AND CORRELATION WITH CLINICAL OUTCOME*

D.M. LOGAN**, J.A. MAROUN†, R. BELANGER††, W.K. EVANS‡
and C.A. IZAGUIRRE‡‡, *Ottawa, Ontario*

NSCLC accounts for 75% of all lung cancers and is the leading cause of cancer-related deaths. The prognosis for NSCLC is poor, because most patients succumb to metastases development, the risk of which cannot be predicted by known NSCLC biological characteristics.

To further study the biological features of NSCLC, we established short-term cell cultures from primary tissue specimens as part of a tissue/cell bank containing primary NSCLC specimens, corresponding cell cultures and clinical outcome data.

During the establishment of the bank cell cultures, we observed a higher than previously reported culture establishment success rate, namely 25/25 NSCLC specimens were successfully established as short-term cultures for at lest four passages. We attributed our success to our modified culture technique, which combines traditional serum-containing media with a serum-free media, ACL-3, specific for NSCLC culture; fibronectin-coated flasks are used to reduce fibroblast growth[1]. It has been reported that ACL-3, which contains epidermal growth factor (EGF) and has a culture establishment rate of 40% within minimal fibroblast growth (a problem with media containing serum)[2]. Thus, our NSCLC cell cultures were started in serum-containing ACL-3 media. However, once the culture became established and the cells reached confluence, the cells were weaned to serum-free ACL-3 to reduce the risk of fibroblast overgrowth. Furthermore, to discriminate NSCLC cells morphologically from fibroblasts, we established a standard panel of commercial antibodies to cytokeratins and vimentin for these evaluations.

---

*CLS-001-2.

**Clinician Scientist, OCTRF Ottawa Regional Cancer Centre, General Division; and Assistant Professor of Medicine, University of Ottawa.

†Head of Medical Oncology, OCTRF Otttawa Regional Cancer Centre; Chief of Staff, Ottawa General Hospital; and Associate Professor of Medicine, University of Ottawa.

††Thoracic Surgeon, Ottawa General Hospital.

‡Chief Executive Officer, OCTRF Ottawa Regional Cancer Centre; Chairman, Division of Medical Oncology, and Professor of Medicine, University of Ottawa.

‡‡Chief, Division of Infectious Immunology, Federal Centre for AIDS, Health and Welfare Canada; and Adjunct Professor of Microbiology and Immunology, University of Ottawa.

Having established the tissue-cell bank and these specific methods, we are testing our hypothesis that: we can predict the ability of NSCLC cells to invade and colonize distant tissues by the presence/absence of some members of the immunoglobulin supergene family, which are responsible of tissue/organ development; and that we can modulate the expression and subsequently cell-metastatic potential by biological response modifiers including interferons.

Our long-term goals are: to determine whether some members of the immunoglobulin supergene family are important in the development of NSCLC metastases, as they are for other tumor types; to determine the role of these molecules in NSCLC metastases development; and to develop therapies to reduce the risk of metastases development, thereby improving NSCLC patients' quality of life and survival.

This project is supported by Ottawa General Hospital Research Fund.

REFERENCES

1. Logan DM, Maroun JA, Belanger R, Evans WK, Izaguirre CA: Establishment of non-small cell lung carcinoma (NSCLC) short term cultures.*Clin Invest Med* 1990; **13:** 4.
2. Brower M, Carney D, Oie H *et al*: Growth of cell lines and clinical specimens of human non-small cell lung cancer in serum-free defined medium. *Cancer Res* 1986; **46:** 798.

ADDITIONAL INVESTIGATIONS

Dr. W.K. Evans, Chief Executive Officer ORCC and Vice-President OCTRF, reports on the following clinical research investigations:

In 1989, 377 patients were entered on clinical trials at the ORCC and 285 were entered on clinical trials in 1990. At present there are 70 active protocols. ORCC staff are participating in NCIC, NSABP, OCOG, pharmaceutical company and local studies. Recently the Centre has joined the Pediatric Oncology Group and the Radiation Therapy Oncology Group. The Centre is participating in adjuvant chemotherapy studies in carcinoma of the breast, colon, and in those of various sarcomas. Combined chemotherapy and radiotherapy protocols for locally advanced disease are underway for carcinomas of the pancreas, head and neck, bladder, prostate, cervix, primary central nervous system lymphomas, and brain metastases for non-small-cell lung cancer. The Centre is participating in chemotherapy studies for advanced metastatic disease in carcinomas of the breast, colon, bladder, prostate, cervix, ovary, lung, sarcomas, multiple myeloma, astrocytomas and oligodendrogliomas. Radiotherapy studies include strontium-89 for breast and prostate carcinoma, intra-arterial yttrium for intrahepatic carcinomas, brachytherapy for high-grade gliomas, preoperative radiotherapy for high-grade gliomas, and radiotherapy combined with hyperthermia. Miscellaneous studies include AREDIA for bone metastases from breast cancer, warfarin for patients with breast cancer on chemotherapy, a randomized study of surgical resection of brain metastases, melanoma excision, *in vitro* studies in Kaposi's sarcoma, atrial naturetic-factor levels in small-cell lung cancer, Phase I studies of didemnin-B, oral menogaril (administered daily for 14 consecutive days), and CI-937, a randomized study of Septra as prophylaxis during leukopenia, a randomized study of Megace in cancer cachexia, bioavailability of 200 mg tablets of MS-Contin, studies of new antiemetics, dexrazoxane as a cardioprotector with epirubicin, and various chemotherapy agents combined with resistance modulators.

PHARMACOLOGY STUDIES

Investigators: D.J. Stewart and R. Goel

Several studies of the pharmacology of antineoplastic agents are underway or are about to be initiated. In recent studies, we have found that, after administration of cisplatin, the dorsal-root ganglion has the highest concentration of platinum of any area in the nervous system. This may help explain the relatively pure sensory manifestation of cisplatin neurotoxicity. In these studies, histopathological evidence of neurotoxicity has correlated with dorsal-root-ganglion platinum concentrations. Studies are being initiated to correlated concentrations of different cisplatin metabolites with cisplatin toxicity, and to determine the effect of various protective agents on relative concentrations of different cisplatin metabolites. Studies have also been initiated to determine whether concentrations of glutathione, glutathione transferase, metallothioneins, and methionine can be correlated with non-small lung cancer resistance to cisplatin.

In an autopsy study of 36 patients who received doxorubicin at some point antemortem, heart doxorubicinol concentrations were higher on average than were heart doxorubicin concentrations. Cardiac concentrations of other metabolites were lower. We did not find epirubicin and epirubicinol in tissues of two patients who received epirubicin antemortem. In eight patients, who had received menogaril antemortem, this agent was found in the tissue of only one patient. The metabolite 7-deoxynogarol was found most commonly in tissues. Studies are underway to correlate cardiac concentrations of anthracyclines with histopathological and antemortem clinical evidence of cardiotoxicity and with various patient characteristics.

In addition, we are participating in pharmacokinetic studies of the anthrapyrazole, CI-937, of intraperitoneal chemotherapy and of a variety of chemotherapy-resistance modulators.

We are also taking part in studies of the pharmacology of dexrazoxane, which is being investigated for its ability to decrease the cardiotoxicity of epirubicin. Its effect on the pharmacokinetics of epirubicin will also be studied.

CLINICAL HYPERTHERMIA OF MALIGNANT DISEASE

Investigators: C.E. Danjoux, L.H. Gerig, G.P. Raaphorst, S. Grimes and A. Ginsburg

Numerous results in the literature have indicated that hyperthermia plays a major role in the treatment of human cancer especially when combined with radiotherapy or chemotherapeutic agents. At the Ottawa Regional Cancer Centre, we are investigating combination of microwave hyperthermia with radiotherapy. To date 20 patients have been treated in this manner. Radiation has been applied using teletherapy or brachytherapy and hyperthermia using an external, 2450 MHz, microwave applicator. The clinical temperature data are being analyzed and converted to thermal dose and these results are compared to tumor response. The results are encouraging and point towards the need to develop or acquire a hyperthermia system for deeper heating.

MEASUREMENT OF PORCINE-TISSUE BLOOD FLOW AND pH DURING HYPERTHERMIA

Investigators: L.H. Gerig, G.P. Raaphorst, C.E. Danjoux, G. Forester and P. Watson

Blood flow plays a major role in the removal of heat during the induction of clinical hyperthermia. In this research project the response of blood flow in various porcine tissues is being evaluated as a function of heating time and temperature. Four methods of blood flow measurements are being employed: (1) blood flow is measured in the arteries by a dye-dilution technique; (2) arterial blood flow measured by electromagnetic technique; (3) blood flow is being measured in tissues by the lodging of radioactive microspheres in capillary beds; and (4) by the measurement of temperature decay in microthermometry probes as a function of time. Initial results indicate that the blood flow can vary as much as 20-fold in response to hyperthermia and that temperatures above 44-45° will cause collapse in the blood-flow response.

INTERSTITIAL HYPERTHERMIA AND BRACHYTHERAPY PROBE

Investigators: L.H. Gerig, G.P. Raaphorst and M. Soubra

In collaboration with Macom Associates, a spiral interstitial microwave hyperthermia probe is being developed to incorporate iridium for iridium-192 brachytherapy. Two approaches are being tested: (1) the construction of the probe with iridium wire which is activated by neutron bombardment; and (2) the construction of a probe with an area which will accept already activated iridium-192 wire. We are doing temperature mapping of the spiral probe performance in tissue-equivalent, phantom material.

DETERMINATION OF THE SPATIAL RESPONSE FUNCTIONS AND TEMPERATURE ERRORS DURING INTERSTITIAL THERMOMETRY

Investigators: L.H. Gerig, J. Szanto, D.S. Salhani and G.P. Raaphorst

From the measured temperature distribution of a cold/warm temperature step, one can determine the spatial response function of the thermometer. Deconvolving the spatial response function of the probe from the measured temperature distribution, the exact temperature can be calculated even for regions of high temperature gradients, e.g., close to large blood vessels, in the tissue treated by hyperthermia.

A numerical model is being developed to determine the errors associated with the heat flow out of the probe through the catheters (radial flow) and along the wires of the probe (axial flow).

DEVELOPMENT OF TWO MICROWAVE APPLICATORS FOR CLINICAL HYPERTHERMIA

Investigators: G.P Raaphorst, L.H. Gerig and M. Soubra

The present clinical trial at the Ottawa Regional Cancer Centre uses a 2450 MHZ microwave system. The clinical data indicates that this system is adequate only for superficial heating and that a deeper heating system is needed. In this regard, a microwave system operating at 915 MHz is being prepared for clinical use. The microwave generator is available, however, there are no applicators. With the collaboration and assistance of the National Research Council and Canadian Astronautics Limited, we are constructing microwave applicators of anew design. These microwave applicators employ a new microstrip technology, which will enable single or multiple microstrip units to be combined in a more flexible applicator. These applicators have constructed and are being tested at the Ottawa Regional Cancer Centre. Low-power tests indicate that they are operating satisfactorily. The next phase will be high-power testing and the evaluation of the heating patterns produced by these applicators through specific absorption rates in phantom materials. Once these projects are completed, the applicators will be available for clinical use.

THERMAL DOSE AND PERFUSION EVALUATION IN CANCER PATIENTS RECEIVING HYPERTHERMIA

Investigators: G.P. Raaphorst, E. Zakhour, L.H. Gerig and C.E. Danjoux

A large amount of thermometry data has been accumulated during the treatment of cancer patients at the Ottawa Regional Cancer Centre. Each patient has had a minimum of 10 and some as high as 30 points of temperature measurement using a microthermocouple thermometry system. This temperature data is being evaluated in terms of the thermal dose delivered to various points of the tissue. The thermal dose calculation is being done according to the algorithms derived from experimental cellular data and described by Saperato *et al.* In addition, the temperature profiles are being analyzed to produce information regarding the change in blood flow in response to hyperthermia. This is accomplished by evaluating the slope of the temperature curves after the power of the microwave applicator has been turned off. At this point the cooling of the tissue should be proportional to blood flow and heat conduction, assuming the conduction term is relatively small compared to the perfusion term, the bioheat equation can be used to evaluate the flood flow rate. These studies indicate an extensive variation in the response of patients in terms of blood flow and thermal dose during hyperthermia.

HYPERTHERMIA AND RADIATION: STUDIES ON INHIBITION OF CELLULAR REPAIR AND THERMO-RADIOSENSITIZATION IN HUMAN NORMAL AND TUMOR CELLS

Investigators: G.P. Raaphorst, M. Feeley, V.F. DaSilva, C.E. Danjoux and L.H. Gerig

It is well known that some cancers respond poorly to radiation and chemotherapeutic agents. One concept is that these cells and tissues are able to repair the damage caused by such therapeutic agents. In this research project, human-derived tumor cells such as those from glioma, melanoma and squamous-cell carcinoma are being evaluated for their radiosensitivity in culture. Attempts will be made to correlate radiation response with ability to repair radiation damage. Hyperthermia is being used to cause radiosensitization and inhibit repair of radiation damage. To date three glioma and four melanoma cell lines are being tested. In addition to survival measurement, cellular repair capacity is being studied through the analysis of DNA polymerases.

MAGNETIC RESONANCE STUDIES OF GLIOMA CELLS AND TUMOR MODELS

Investigators: G.P. Raaphorst, D. Wilkins, J. McTavish, I. Smith and J. Saunders

p^{31} Spectroscopy. Many studies have shown that the stress caused by cancer therapeutic agents can cause changes in the high-energy phosphorous metabolites with cells. In this study, we are investigating the P^{31} spectroscopy of rat glioma cells *in vitro* and *vivo*. To date experimentation with the rat 9L cell line *in vitro* in a perfusion apparatus shows a low level of PCR and high levels of ATP in these cells. A special probe is being constructed to evaluate the P^{31} metabolites in a brain tumor produced by implenting these cells in the brain of Fisher-444 rats. Both cells *in vitro* and in the tumor are being evaluated for the responses to hyperthermia, radiation, chemotherapeutic agents and combinations of these. Localized spec-

troscopy has been achieved on volumes of about 1-15 cc and we are working to reduce the volume to about 0.5 cc.

Microimaging. We are using a set of microimaging gradient coils, developed at NRC, to produce high-resolution images of the rat 9L brain tumor. Image resolution is to a voxel size of 40x40x150 micrometers. One can discern detailed tumor morphology and thus evaluate effects of treatment agents on early changes in brain and tumor morphology. These results show clear ability to characterize tumor size and its response to therapy. In addition, microstructure such as proteinaceous cysts within the tumor also can be measured.

PULSE SEQUENCE DEVELOPMENT FOR CLINICAL MRI

Investigators: I.G. Cameron and R.M. Kroeker

Presaturation Techniques. Presaturation is an attempt to eliminate artifacts arising from the motion of various organs during the acquisition of image data. Motion of the chest wall, cardiac motion, and flowing blood commonly appear as a pattern of regular bands of signal intensity in the MRI. Presaturation uses specialized radiofrequency pulses which eliminate signals from the regions producing the artifacts.

A number of programs have been written that allow the clinician to adapt regular imaging sequences to ones which implement presaturation. A total of 12 imaging methods are available, including methods such as spin echo multislice (SEM), fast low-angle shot(FLASH), fast imaging with steady precession (FISP), and a number of gradient motion refocussing (GMR) sequences.

GMR Sequences. It is an imaging technique that compensates for artifacts arising from constant velocity and/or constant acceleration flow in MRI. Commonly used for imaging the head, GMR helps to eliminate the pulsatile flow artifacts from CSF in the ventricles. We have five sequences into which GMR has been incorporated in one direction (the read gradient direction) and we are extending these sequences so that they have GMR in the slice select direction as well.

Spin Diffusion Sequences. These sequences are sensitive to the diffusion of water. Tissues that exhibit a high degree of diffusion appear dark, while other tissues are bright. Such techniques are being developed to assess intrauterine growth retardation in pregnant women, not assessed by the ultrasonic profile. This method relies on the secondary effects of placental insufficiency on the fetus, such as fetal movement and sequential growth. However, since placental degeneration leads to increased resistance to blood flow in the fetal placental vessels, MRI spin diffusion techniques may be a more sensitive method for a direct assessment of placental health.

CLINICAL SPECTROSCOPY

Investigators: I.G. Cameron, R.M. Kroeker and A. Rutter

p^{31}Spectroscopy. p^{31} *in vivo* spectroscopy techniques and protocols form the basis of several clinical research projects and several more, which are planned for the near future. In these techniques, we obtain p^{31} NMR spectra from specific regions of a patient's body, which are selected by positioning a surface (pick-up) coil over that part of the body. Normally, these spectra are used to monitor high-energy metabolites such as ATP, however, other things such as tissue pH also can be measured accurately with this procedure.

^{19}F Spectroscopy. Most of the necessary hardware to do ^{19}F *in vivo* spectroscopy has been installed on the imager. The only missing part, the receiver coil, will depend on the exact nature of the research projects for which the spectroscope will be used. We are gathering the information necessary to make a decision on the design of the coil. This technique promises to be useful in monitoring the uptake of fluorinated rugs in patients.

^{1}H Spectroscopy. Recently we received a software package from Siemens which will allow us to do localized *in vivo* ^{1}H spectroscopy. It is being tested on phantoms and should be ready for use on patients in the near future. Since the body contains so many hydrogen-containing compounds, this technique promises to provide a wealth of important chemical information.

Chemical Shift Imaging (CSI). We are studying CSI, a technique by which images can be generated from a particular line in a spectrum rather than using the full signal for the nucleus. We have a one-dimensional version of CSI which gives a series of spectra from different depths within a cylindrical volume defined by the surface coil. We are working on a three-dimensional version of CSI which uses a head coil rather than a surface coil. In the meantime, however, the one-dimensional version will be used in a study of untreated brain tumors.

USING p^{31} SPECTROSCOPY TO SCREEN FOR MALIGNANT HYPERTHERMIA

Investigators: G. Allen, A. Ashley, L.I. Avruch, I.G. Cameron,
R. Deslauriers, A. Rutter and J.K. Saunders

Malignant hyperthermia (MH) is a potentially fatal, genetic disorder which causes the body temperature to rise uncontrollably under general anesthetic. Currently, a biopsy of muscle tissue—an inconvenient and somewhat painful procedure—is the best way of screening for MH. p^{31} *in vivo* magnetic resonance spectroscopy shows great promise as a quick and painless way of screening for MH. Recently, we have applied to the Ethics Committee of the Ottawa General Hospital to run trials using volunteers from the Ottawa chapter of the MH Society.

NMR SPECTROSCOPIC EVALUATION OF UNTREATED BRAIN TUMOR PATIENTS

Investigators: H. Hugenholtz, A. Girard, D.J. Stewart, V.J. Montpetit,
L. Avruch, G.P. Raaphorst, I. Cameron, J.K. Saunders and I.C.P. Smith

The prognosis and treatment of human brain tumors is influenced by such variables as histological type, malignancy and degree of necrosis within the tumor. Currently such information requires surgery with its attendant risks. However, studies with tumor extracts, animal tumor models and a few human tumors have shown that magnetic resonance spectroscopy (MRS) can distinguish several classes of tumor from one another and from non-tumor tissue. Techniques have been developed which enable MR spectra to be obtained from anywhere in the body and from localized volumes of only 5 cm^3. By the time they become symptomatic and visible on CT scans, most human brain tumors exceed that volume. Therefore we intend to apply our earlier experience with MRS to patients with brain tumors who are scheduled for surgical removal. Just before operation, such consenting patients will have proton and phosphorus spectra recorded from their tumors using the MR spectrometer at the Ottawa General Hospital. The tumor tissue removed at operation will be studied in detail and categorized according to type and degree of necrosis. Small representative samples of the tumor tissue, removed at operation also will be studied by *in vitro* MRS at the National Research Council of Canada, so as to compare the preoperative *in vivo* studies with *in vitro* studies of the actual tumor tissue. It is anticipated that we will identify common spectroscopic features among certain classes of tumor and among tumors with different degrees of necrosis, providing evidence to support the potential of MRS as a tool to characterize human brain tumors and to monitor and modify their treatment.

STUDY OF LONIDAMINE AS A RADIOSENSITIZER, THERMOSENSITIZER AND CHEMOSENSITIZER OF RODENT AND HUMAN CELLS IN CULTURE

Investigators: G.P. Raaphorst, C.E. Danjoux, J. Maroun, M. Feeley and D. Ko

Lonidamine, a compound which has been used as a contraceptive agent, specifically as a spermaticide, also may have therapeutic effectiveness in cancer. We are testing the effect of lonidamine itself on rodent and human cells. Also, we are combining it with radiation to measure its radiation sensitization properties and to determine whether it can inhibit the repair of radiation damage. In addition, we are evaluating its properties as a thermal sensitizer and sensitizer when combined with other chemotherapeutic agents. We have completed studies on lonidamine combined with radiation on various human-cell and rodent-cell lines, studies on lonidamine combined with cisplatinum show that it enhances the killing effect of radiation in squamous cell carcinoma of the head and neck. Lonidamine was found to improve response of lung-tumor cell lines to cisplatin, but only at very high concentrations.

THERMO-CHEMOSENSITIZATION ON HUMAN RESISTANT TUMOR CELL LINES

Investigators: V. DaSilva, M. Feeley and G.P. Raaphorst

Hyperthermia plays a major role in chemosensitization. We are evaluating the effect of hyperthermia on several chemotherapeutic agents tested in resistant human tumor-cell lines. In human glioma-cell lines, we have shown that response to agents such as cisplatinum, BCNU, AZQ and SHM can be increased by the application of hyperthermia. In addition, studies are being done with a BCNU-resistant variant to determine whether hyperthermia can overcome such resistance and results to date indicate that moderate thermosensitization can be achieved. This strategy may apply to resistance to other chemotherapeutic agents. We are doing further work to evaluate resistance to cisplatin and thermo-chemosensitization.

STUDY OF RADIOSENSITIVITY OF LYMPHOCYTE AND LYMPHOBLAST CELLS DERIVED FROM PATIENTS UNDERGOING CANCER THERAPY

Investigators: C.E. Danjoux and associates, G.P. Raaphorst and M. Feeley

It has been assumed that, during therapy, radiation doses delivered to patients in general are limited by the response of a subpopulation which are more sensitive than the mean or to the response of another subpopulation which may be more resistant. Normal tissue responses in such patients set the upper limit for radiotherapy doses in all patients. To determine whether the human population exhibits such heterogeneity, we are determining the radiation response of lymphocytes and lymphoblasts derived from patients at the Ottawa Regional Cancer Centre. These studies are being done at Atomic Energy of Canada, in collaboration with N. Gentner and D. Morrison, who developed and perfected the technique for such tests. With these data, we hope to demonstrate whether such a heterogeneity in radiation response exists and then to determine in advance which patients are being treated to their optimum dose and which may receive safely more optimum levels of radiation.

HIGH DOSE RATE RADIATION OF HUMAN CELLS

Investigators: J. Cygler, M. Feeley, G.P. Raaphorst, N. Klassen and C.K. Ross

We are studying the response of human glioma cells to high dose rates of radiation under oxic and anoxic conditions, using electron beams of duration 40 ns and 2.5 s. These results are being compared with those from Co-60 studies. Using our improved technique for irradiation of the cells under anoxic condition, we have found an OER found of 2.8, a figure that agrees with commonly accepted data for human-cell lines.

THERMAL RADIOSENSITIZATION FOR LOW-DOSE-RATE IRRADIATION IN HUMAN TUMOR CELL LINES

Investigators: G.P. Raaphorst, D. Heller and M. Feeley

Low-dose-rate irradiation is used in many brachytherapy procedures because, under such conditions, cells are able to repair sublethal damage. In tumors whose cells have a high capacity for such repair, this may reduce the effectiveness of brachytherpay. We are evaluating hyperthermia as a radiosensitizer and a repair inhibitor for low-dose-rate radiotherapy in human melanoma and glioma cell lines. These cells are know to be resistant and have a large capacity for repair. The cell irradiation is being constructed and cell growth is being characterized.

MEASUREMENT OF MEGAVOLTAGE *BREMSSTRAHLUNG* SPECTRA FROM 5-40 MeV ELECTRONS ON THICK TARGETS

Investigators: B. Faddegon, D.O.W. Rogers, C.K. Ross and G.P. Raaphorst

Physicists and therapists need electron *bremsstrahlung* cross-sections for a variety of applications. However, few measurements are available and the calculations only are accurate to about ±10%. The purpose of this project is to measure the thick-target *bremsstrahlung* spectra of 5-40 MeV electrons from a linear accelerator, differentially in energy and angle for targets covering a wide range of atomic number. We will compare measured spectra to Monte Carlo spectra to establish the accuracy of this calculation approach.

Already, the measurement system has been used to obtain aluminum and lead targets at normal incidence (0° and 10°). Measured spectra shapes and relative cross-sections agree well with the Monte Carlo results. Improved energy calibration techniques have been explored and employed. Most recently we have achieved the capability of absolute cross-section measurement to better than a few percent. Soon a comprehensive set of cross-sections should be available.

COMPUTER-CONTROLLED RADIOTHERAPY

Investigators: D. Salhani, L. Gerig, G.P. Raaphorst, S. Samant and A. Girard

The therapeutic effectiveness of radiotherapy can be improved by conforming the radiation beam precisely to the tumor volume. Ideally we could achieve this by knowing the exact tumor volume and controlling the motions and output of a linear accelerator to optimally radiate such a volume. We are planning experiments on computer-controlled radiotherapy using the new Siemens KD-2 linear accelerator being installed at the General Clinic. Elsewhere, we have described several features of this large project which we will work on. These include the development of an overall supervisory computer system and a system to optically monitor patient position. We will work on an automatic setup and verification and on collision avoidance algorithms, couch control and interfacing with treatment planning and imaging systems.

MODIFICATION BY A GOLD BACKING OF DOSE RATE FROM IODINE-125 SEEDS

Investigators: J. Cygler, D.W.O. Rogers, J. Szanto and M. Soubra

Iodine-125 (I-125) is commonly used in brachytherapy of eye cancer. The treatment is delivered by application of special eye plaques consisting of a gold and plastic shield which sandwich the I-125 seeds. Due to a high dose gradient in the vicinity of the I-125 seeds, accurate dosimetry is extremely difficult and contrary reports have been made concerning the influence of gold on the dose close to the seed.

We performed dosimetry measurements employing a small p-type shielded diode (active surface 1 mm^2) and an RFA-7 Therados dosimetry system which enables positioning with a nominal accuracy of 0.1 mm. Our data confirm that the presence of gold changes the dose in the vicinity of the I-125 seed (6702 type) by a magnitude and sign which depend on the medium and on the distance from the seed. Our results are in general agreement with Monte Carlo calculations. A paper describing this study has been accepted for publication in *Medical Physics*.

THE OMEGA PROJECT: DEVELOPMENT OF AN ELECTRON-BEAM TREATMENT PLANNING SYSTEM USING MONTE CARLO TECHNIQUES — OTTAWA-MADISON ELECTRON-GAMMA ALGORITHM

Investigators: T.R. Mackie, D.W.O. Rogers, S.S. Kubsad, A.F. Bielajew, T.J. Kinsella, B.A. Faddegon and J. Cygler

The goal of this project is to develop a 3-dimensional dose-calculation algorithm for electron-beam radiotherapy planning employing direct Monte Carlo simulation of the radiation transport in the patient. We plan to do extended validation of the technique using variety of experimental phantoms and clinical examples before implementation in the Centre. This project is a collaborative effort between University of Wisconsin, National Research Council of Canada, and Ottawa Regional Cancer Centre.

CLINICAL EVALUATION OF SOLID STATE DOSIMETRY (MOSFET)

Investigators: J. Cygler, M. Soubra, G. MacKay, I. Thompson and A. Ribes

We have investigated a new type of direct-reading semiconductor dosimeter as a radiation detector for photon and electron therapy beams of various energies. This device is based on the measurement of the threshold voltage shift in a custom-built, metal-oxide semiconductor transistor (MOSFET). This voltage is a linear function of absorbed dose. The extent of the linear region increases with the increase of the bias voltage. The energy response of this detector is largely enhanced for low photon and electron energies. However, by incorporating an appropriate filter in the dosimeter, we have achieved a much flatter energy response. The modes of operation give this device many advantages, for example, continuous monitoring during irradiation, immediate reading and permanent storage of total dose after irradiation. The availability and ease of use of these MOSFET detectors make them very promising in clinical dosimetry.

CHARACTERISTICS OF ELECTRON BEAMS PRODUCED BY KD-2 LINEAR ACCELERATOR

Investigators: J. Cygler and other physicists

Electron beams from the Siemens KD-2 linear accelerator have been characterized for open applicators for all available energies, i.e., 6, 9, 11, 13, 17, and 20 MeV in a homogeneous water-like phantom. We have determined initial angular spread of the beam for each electron energy from measurements in air. In progress are studies for irregular and partially blocked fields.

DIGITAL IMAGE PROCESSING

Investigator: J. Szanto

We were developing an image correlation algorithm which will allow the comparison of a portal image with the corresponding simulator film. The images are digitized into the computer and the correlation is performed via fast Fourier algorithms.

SMALL BEAM RADIOTHERAPY

Investigators: J. Szanto and L. Gerig

An analytical method developed to describe small radiotherapy beams (1 cm to 4 cm) is the basis of our treatment planning system, which can handle any number of coplanar beams in any configuration on the contour of a skull. Because our beam model is 3-dimensional, we will use it in the development of a 3-D small-beam treatment planning system.

BEAM PROFILE – ISODOSE CONVERSION BY COMPUTER

Investigators: J. Szanto and L. Gerig

We have developed a computer program in ASYST, which creates isodose distribution of radiotherapy beams using their measured profile data. The profiles have to be measured at least at every 2 cm. This method achieves a noise-free, high-resolution isodose plot and cuts the measurement time considerably.

GENERALIZED LEAST-SQUARES ANALYSIS OF BEAM DATA

Investigators: S. Salhani, J. Szanto and L. Gerig

The primary application of this method is to determine a functional form for measured beam data. The functional representation lends itself well to treatment planning calculation and treatment-time algorithms. Function representations have been achieved for both photon and electron data from KD-2 with excellent results.

3-DIMENSIONAL REFERENCING OF OBJECTS IDENTIFIED ON THE CT-SCAN OR X-RAY FILMS

Investigator: A.A. Kania

Radiation of interstitial brain requires transformation of the data obtained from CT scans or X-ray films into operational rules of setting the stereotaxic reference frame. This transformation requires complicated calculations in 3-dimensional geometry. Commercial software is available but only in a sealed form, attached to a dedicated hardware unit, which is an HP programmable calculator. Other research workers are investigating the use of localizers (the localizer ring and intercranial localizing box) as a stand-alone (hardware and computational) system. Our objective is to write software which would relate data from localizers to physical 3-dimensional co-ordinates of the volume of interest (a tumor in a brain).

PHOTOFRIN ACTIVATION BY IONIZING RADIATION

Investigators: L. Eapen, D. Singleton and H. Birnboim

We are doing experiments to determine if ionizing radiation can activate the compound photofrin with a view to exploring a different approach to photodynamic therapy. The experiments are designed to detect singlet oxygen production using an aniline-dye-based, singlet-oxygen-scavenger system. By this means, we hope to determine the spectro-photometric changes in the photofrin molecule following ionizing radiation and to assess cellular cytotoxicity produced by photofrin light and ionizing radiation.

Northeastern Ontario Regional Cancer Centre

CLINICAL INVESTIGATIONS

Dr. R.E.T. Corringham, Chief Executive Officer NEORCC and Vice-President OCTRF, reports on the following clinical research investigations:

In 1990, 72 patients were entered on clinical trials at the Northeastern Ontario Regional Cancer Centre. Presently, 22 active clinical studies are accruing patients. These studies include adjuvant chemotherapy for patients with breast cancer and colorectal carcinoma and chemotherapy for patients with advanced or metastatic breast cancer, multiple myeloma, colorectal carcinoma, non-Hodgkin's lymphoma, small-cell and non-small cell lung cancer and lymphoid malignancies. As well as participating in Phase I, II and III NCIC, NSABP and drug company studies, our centre conducts its own in-house studies including chemotherapy ± autologous blood, progenitor-cell transplantation for patients with small-cell lung cancer, non-Hodgkin's lymphoma, metastatic breast cancer and multiple myeloma. Studies are also being conducted of new antiemetics and also the use of Port-a-caths. Studies combining chemotherapy with radiation in patients with cervix carcinoma will be activated early in the new year.

MODULATION OF T-CELL ONTOGENY WITH HEMATOPOIETIC GROWTH FACTORS: *IN VITRO* AND AFTER STEM-CELL TRANSPLANTATION

Investigator: A.D. Ho

Similar to other cytokines, the hematopoietic growth factors such as rhGM-CSF and rhG-CSF might have pleotropic effects on the complex cytokine network in the living organism. Although rhGM-CSF was believed to interact with cells of the myeloid lineage alone, recently it has been shown to exert effects on leukemic cell lines derived from undifferentiated T-lymphocytic leukemia and on normal interleukin-2 (IL-2) driven T-cells. In patients with malignant lymphoma, we have shown that there was a vigorous rise in soluble IL-2-receptor (sIL-2R) antigen within the first 36 hours after administration of rhGM-CSF. Parallel to this increase, there was also a significant increase in cells expressing CD25 within the CD3+ subpopulation, elevation in CD4+ cells and in the absolute lymphocyte count. Thus these observations have indicated that rhGM-CSF can modulate the activation, proliferation, and differentiation of T-lymphocytes *in vivo*. In another project, the effects of rhGM-CSF and rhG-CSF on IL2-driven, normal T-lymphocytes were studied *in vitro*. Preparations of T-cells from peripheral blood of normal donors were incubated with IL-2 alone, rhGM-CSF or rhG-CSF alone, or with IL-2 plus rhGM-CSF or rhG-CSF. As determined by the percentage of cycling cells, proliferative activity was twice as high in the cultures incubated with both rhGM-CSF-IL-2 or rhG-CSF-IL-2 than in those incubated with the growth factors, IL-2 or medium alone. There was also a significant increase in absolute numbers of CD4+, of CD8+ and CD25+ cells and the corresponding soluble antigens in cultures containing rhGM-CSF/IL-2 or rhG-CSF/IL-2. Based on these results, we will continue to assess the effects of other hematopoietic growth factors on activation, proliferation and functional integrity of the lymphocytes. Parallel to these *in vitro* experiments, we will study the impact of clinical administration of rhGM-CSF on the functional integrity of lymphocytes from patients treated with this growth factor. The administration of such factors might enhance immune-response recovery after stem-cell transplantation.

SUPER-DOSE INTENSIFIED CHEMOTHERAPY WITH AUTOLOGOUS BLOOD PROGENITOR CELL TRANSPLANTATION AND GROWTH FACTOR SUPPORT FOR PATIENTS WITH SOLID TUMORS

Investigator: A.D. Ho

Numerous studies have shown that high-dose chemotherapy (with or without total body irradiation) followed by autologous bone-marrow transplantation can improve response duration and survival of patients with advanced solid tumors. This strategy is based on the observation that dose intensity of the administered cytotoxic agents is an important determinant of treatment outcome. For most cytotoxic drugs, myelosuppression—the dose-limiting toxicity—can be circumvented by autologous progenitor-cell support. Conventionally, the progenitor cells or stem cells are obtained from the bone marrow. Recently it has been shown that progenitor cells enriched from the peripheral blood can also be used as an alternative to bone-marrow progenitor cells. Originally this approach was proposed for patients after extensive irradiation to the sites for bone-marrow harvesting. We have demonstrated that the rate of hematopoietic reconstitution with peripheral-blood progenitor cells can be as good as or even more rapid than with bone-marrow progenitor cells. Moreover we have shown that, in patients with non-Hodgkin's lymphoma, rhGM-CSF alone induces a significant increase in the number of circulating hematopoietic progenitor cells which then can be used to restore hematopoiesis after super-dose chemotherapy. In a small series of patients with advanced and heavily pretreated Hodgkin's disease, this procedure has proven to be effective. Based on these results, we have proposed a new concept that combines the induction chemotherapy regimen with peripheral-blood, stem-cell harvest in the phase of leukocyte recovery. All clinical and laboratory preparations have been made and a study is underway of the feasibility of administration of rhGM-CSF to enhance hematopoietic reconstitution and progenitor-cell yield after each cycle of induction chemotherapy. After collection of sufficient number of peripheral progenitor cells, we will administer a super-dose pretransplant regimen, which is adapted to the primary tumor. The cryopreserved, progenitor-cell preparation will be reinfused. The objectives of this project are: (1) to assess the efficacy of super-dose chemotherapy as primary treatment in patients with metastatic breast cancer and in patients with poor-risk, non-Hodgkin's lymphoma; (2) to assess the role of peripheral-blood, progenitor-cell support combined with rhGM-CSF after super-dose chemotherapy in accelerating hematopoietic reconstitution; (3) to assess the role of rhGM-CSF after conventional induction chemotherapy to enhance peripheral-blood, progenitor-cell yield for transplantation; and (4) to assess the influence of successive chemotherapy cycles on the progenitor-cell yield after each cycle.

Thunder Bay Regional Cancer Centre

CLINICAL INVESTIGATIONS

Dr. J.F. Kotalik, Chief Executive Officer TBRCC and Vice-President OCTRF, reports on the following clinical research investigations:

CLINICAL TRIALS

We continue to support co-operative clinical trials by screening every new patient registered at the TBRCC for eligibility for one of the investigative protocols. Currently seven Canadian co-operative trials and 15 in north central cancer treatment group trials are open in our Centre. In 1990, we entered 53 new patients in clinical trials, which represents an increase of 15% comparing with 1989. The main trials were those for advanced colorectal malignancy, adjuvant breast therapy for node-negative cancer and adjuvant therapy for post-menopausal Stage II breast carcinoma. Also we are fully committed to the Ontario Clinical Oncology Group trial, which examines the role of warfarin in Stage IV carcinoma of the breast. We entered 21 patients into symptom-control trials examining the alleviation of nausea and vomiting associated with chemotherapy.

Our group is now investigating the possibility of joining a radiotherapy oncology group so we can participate in trials in which the treatment is radiotherapy.

MEDICAL PHYSICS

A project involving comprehensive characterization of dosimetric parameters of clinical electron beams produced by the Mevatron-KD linear accelerator was completed recently and presented at the meeting of the American Association of Physicists in Medicine in St. Louis, MO. We have submitted a detailed paper for publication.

We have completed the software for our prototype, computerized, patient-contouring device and have begun work on the mechanical aspects of this device. We hope that this device will be in clinical testing in the spring of 1991.

An evaluation of our quality control program will look at the dosimetric and geometrical parameters of radiation-generating devices and examine their stability as a function of time. This project, which is in the initial stages, will require a great deal of time and effort to bring it to fruition.

We are continuing the work on radiation effects on semiconductor devices described in last year's report. Two final-year students in electrical engineering have completed their projects in this area and two more have started. This work is carried out in collaboration with Dr. D. Barry, Electrical Engineering, Lakehead University.

The OCTRF has approved a training position at the junior physicist level and we hope this appointment will enhance the modest research effort in the department and perhaps help to alleviate somewhat the shortage of trained medical physicists.

In the summer of 1990, Dr. Ian Smith, a senior scientist from the National Research Council of Canada, gave a seminar on the potential of MRI/MRS in the diagnosis and management of malignancies. The aim was to stimulate interest in this modality among the local medical community. Siemens Electric Limited provided funding for this meeting.

We enjoyed having Dr. J.C.F. MacDonald, a seasoned colleague with us, as a locum physicist during the month of September.

The activities of the Department of Physics continue to be limited by shortages of staff, facilities and space, but we hope this will be remedied in the near future once new positions are approved. The research effort in the department continues to benefit from funding provided by the H.E. Johns Summer Studentship and SEED programs for which we are grateful. In addition to the obvious research benefits, these two funding sources help to strengthen our academic affiliation the Department of Physics of Lakehead University, from whence we draw our students.

PSYCHOLOGICAL ONCOLOGY

A number of preliminary investigations were made possible by Dr. Scott Sellick's adjunct appointment to the Department of Psychology of Lakehead University. During 1990 we mailed a survey to approximately 300 physicians in Northwestern Ontario concerning attitudes toward the role of the psyche in medical practice. Although the short questionnaire allowed for a full range of responses and some physicians highly endorsed the role of the mind in illness and healing, while others strongly rejected mind-body interaction, the investigators could not account for differences in attitudes. Neither age, sex, country of training, years in practice (urban, rural), nor area of specialty were discriminating variables. Another graduate student is measuring medication compliance among breast cancer patients who have been prescribed tamoxifen. One of four earlier pilot projects is being considered for a joint centre study and we will enlist the support of other centres in seeking external funding for collaborative psychosocial research.

Toronto-Bayview Regional Cancer Centre

CLINICAL INVESTIGATIONS

Dr. R.D.T. Jenkin, Chief Executive Officer T-BRCC and Vice-President OCTRF, reports on the following clinical research investigations:

SIGNAL TRANSDUCTION PATHWAYS IN MALIGNANT MELANOMA

Investigator: N. Iscoe

In Canada, the incidence and mortality of cutaneous malignant melanoma are increasing more quickly than those of any other malignancy except lung cancer in women. In view of the current and projected incidence of this disorder, it is of particular concern that medical therapy for advanced disease remains ineffective. The objective of my research program are to define the signalling pathways which regulate melanocyte proliferation and to define how these pathways are disrupted in malignant melanoma.

The proto-oncogene *c-kit* encodes a transmembrane receptor protein which plays a pivotal role in normal melanocyte development. It is therefore important to determine the expression and function of this protein in both normal and transformed melanocytes. Our preliminary studies have shown that transformation of human melanocytes frequently is accompanied by changes in *c-kit* expression. To define the role of *c-kit* in human malignant melanoma, we are studying expression of this proton-oncogene in both melanoma cell lines and tumor samples. In addition, we will test the hypothesis that *c-kit* expression plays a direct role in melanocyte transformation.

Basic fibroblast growth factor (bFGF) may play an important role in melanocyte transformation. Normal melanocytes, unlike malignant melanoma cells, do not proliferate *in vitro* using routine media supplemented with serum. However, addition of bFGF permits the growth of melanocytes in culture and expression constructs, which contain the bFGF gene, will transform melanocytes *in vitro*. Since it has also been shown that malignant melanoma cells express this growth factor constitutively, and because normal melanocytes do not produce detectable levels of bFGF, it is important to evaluate the role of this factor in melanocyte growth *in* *vivo*. To target the expression of this gene to melanocytes, we will use a construct containing a full length bFGF cDNA driven by the murine tyrosinase promoter to generate transgenic mice.

The protein tyrosine kinases comprise a family of enzymes, which mediate signals involved in the regulation of cell proliferation. Many of these proteins, when mutated or expressed constitutively, possess oncogenic potential. We have used a recently described polymerase chain-reaction technique to identify protein-tyrosine-kinase sequences in both normal and transformed human melanocytes. Studies are under way to further characterize the subset of protein-tyrosine kinases, which are differentially expressed in melanomas relative to their untransformed counterparts.

INTRAPERITONEAL ADMINISTRATION OF RADIOLABELLED ANTIBODIES

Investigators: R. Buckman, P. Shaw, C. De Angelis, A. Covens, R. Osborne, G. Mills, M. Woo, R. Reilly, J. Kerr, J. Law, H. Begley, E. Groves, R. Baumal and A. Marks

Our group has continued to investigate the use of monoclonal antibodies (MoAb) as carriers of radioisotopes in the therapy of drug-resistant malignant effusions. The MoAb 2G3 is almost identical to the MoAbs HMFG-1 and HMFG-2 employed in several clinical trials. Like them, 2G3 recognizes an antigen—a mammary mucin present in high amounts ($3\text{-}4\text{x}10^6$ antigenic sites per cell, as demonstrated by immuno-electron microscopy) on the surface of most malignant cells in all effusions of breast or ovarian origin. Like the HMFG antigen, the 2G3 antigen also is shed from the cell surface and is measurable in ascites and serum.

We now have treated 13 patients and have demonstrated that targeting of MoAb to the cell surface is unsatisfactory due to the presence in the supernatant of shed antigen. This may account for the disappointing clinical results achieved even at total doses of 150 mCi of ^{131}-I. The temporary palliation achieved in three patients may be attributable to MoAb complexed with soluble antigen acting as radiocolloid.

This work now continues with the search for a more suitable antigenic target, an antigen that is not shed from the cell surface and which may be associated with cells of the highest clonogenic potential. Growth-factor receptors may be suitable candidates and the group now is investigating a new panel of MoAbs directed against growth factor receptors (including EGF, *neu* and TGF-alpha) to identify a suitable candidate MoAb for future clinical trials.

This work is supported by a grant from the Physicians' Services Incorporated Foundation.

THE ROLE OF *NEU* ONCOGENE AMPLIFICATION AND FLOW CYTOMETRIC MEASUREMENTS AS PROGNOSTIC VARIABLES IN PREDICTING RELAPSE AND SURVIVAL IN WOMEN WITH AXILLARY-NODE-NEGATIVE BREAST CANCER

Investigators: K.I. Pritchard and M.E. Trudeau, principal investigators, with L.L. Andrulis, W.H. Hanna, H.L. Lickley, G.B. Mobbs, D. Murray and C.A. Sawka

The most important predictor for relapse in breast cancer is the presence of metastatic disease in axillary lymph nodes at the time of initial surgery. Although women with axillary-node-negative disease have a lower risk of relapse than their node-positive counterparts, a proportion of node-negative women will relapse and ultimately die of breast cancer. It is important to identify this subgroup of node-negative women at high-risk of relapse because they should be targeted for trials of adjuvant therapy.

The principal investigators, Drs. Pritchard (T-BRCC) and Trudeau (Women's College Hospital) are analyzing the prognostic importance of *neu* oncogene amplification and measures of cancer-cell activity (flow cytometric measurement of %S phase and DNA content) in 432 women with node-negative breast cancer. These women are a subset of the Henrietta Banting Breast Centre database, which consists of all women with primary breast cancer surgery done at Women's College Hospital in Toronto from 1977-1986 inclusive. In addition to these experimental factors, other factors believed to be prognostic for relapse and death, will be examined by multivariate analysis. The Ontario Ministry of Health has allocated $126,938 for this study, which began in April 1989 and will be completed in March 1991.

A PROSPECTIVE RANDOMIZED STUDY OF TAMOXIFEN COMPARED TO TAMOXIFEN PLUS SIX MONTHS OF CMF IN POSTMENOPAUSAL WOMEN WITH AXILLARY NODE-POSITIVE BREAST CANCER

Investigators: K.I. Pritchard, principal investigator, with S. Fine and A.H.G. Paterson

A co-operative group from Toronto and Edmonton designed this prospective randomized study of breast cancer in postmenopausal, axillary-lymph-node-positive women. Women were randomized to receive either tamoxifen 30 mg daily for two years, or tamoxifen 30 mg daily for two years plus cyclophosphamide, methotrexate and 5-fluorouracil (CMF) every eight weeks for eight treatments - about six months. The original sample size was 300 patients. Initial funding was obtained from the Medical Resarch Council of Canada (MRCC). Within a few months of the trial's opening in 1984, the Clinical Trials Group of the National Cancer Institute of Canada (NCIC), under the leadership of Dr. Joe Pater, joined the core investigators for a multicentre, cross-Canada study with data co-ordination by the Clinical Trials Group office. Dr. Pritchard is study chairman. The MRCC continues to provide core funding with NCIC.

Because this group of patients has an extremely favorable survival the group decided to increase the sample size to 700 patients to improve the power of the study. The accrual target was reached as of December 1990 and analysis will be carried out in mid-1991 under the guidance of Drs. Pater and Pritchard.

BIOLOGIC PROGNOSTIC FACTORS IN NON-HODGKIN'S LYMPHOMA

Investigators: N.L. Berinstein, C. Sawka, M. Reis, A. Dembo, R. MacKenzie, A. Willan, J. Srigley, P. Pinkerton and B. Ngan

This is a prospective study to analyze a number of novel biologic factors in new patients with non-Hodgkin's lymphoma. We will determine whether these novel biologic factors can be useful in predicting prognosis. Some of the biologic factors, which will be studied, include: detection of occult disease, PCR analysis of bone marrow and peripheral blood, the study of immunoglobulin-variable gene utilization in B-cell lymphoma, the study of oncogene activation in these lymphomas, analysis of immunoglobulin and T-cell receptor-gene status and the phenotypic analysis of lymphoma cells and host effector cells.

This study has been funded by the Medical Research Council of Canada.

DETECTION OF MINIMAL SUBCLINICAL DISEASE IN NON-HODGKIN'S LYMPHOMA BY PCR AMPLIFICATION OF T(14:18)

Investigator: N.L. Berinstein

This project will use highly sensitive molecular technology to determine whether the peripheral blood and bone marrow of patients undergoing staging for non-Hodgkin's lymphoma contains subclinically detectable lymphoma. We will follow prospectively the clinical course of these patients and determine whether the results of these tests can be useful in creating a more accurate prognostic model.

DOSIMETRY OF Nd-YAG LASER PHOTOILLUMINATION OF THE BRAIN

Investigators: R. Siwek, D. Wyman, C. Swift, B. Wilson and S. Schatz

A series of rabbits were anesthetized and underwent a frontoparietal craniectomy. The dura mater was incised and retracted to expose the brain surface. A single optical fibre was inserted into the brain with either two or no thermocouples. The fibres were inserted to a depth of about two centimeters. Exact positioning was achieved using a three-dimensional, translational jig. We used various power settings and photoillumination times. The rabbits were sacrificed at the end of irradiation or after 48 hours. During the 48 hours after irradiation, the rabbits showed no signs of distress and were neurologically inact. The brains were placed in formalin and later examined histologically to verify the extent of damage. Effects of different fibre tips (spherical, diffusing and cut-end) were investigated.

THE DENSITY SCALING METHOD FOR DOSIMETRY OF RADIOLABELLED ANTIBODY

Investigator: M.K. Woo

This project will investigate alternative methods for radioimmunotherapy (RIT) dosimetry. The present method, MIRD (medical internal radiation dose) dosimetry, is based on tabulated data calculated for a fixed geometry (the "reference man") and is in wide use in nuclear medicine. MIRD dosimetry is grossly inadequate for use in RIT under certain conditions but, because it is the only schema available, it is used clinically at our institution. We will investigate the use of the density scaling method, based on Monte Carlo computer simulations for various inhomogeneity configuration. The Monte Carlo codes EGS4 and ITS are run on both a MicroVax and CRAY computers.

DOSIMETRY OF RADIOLABELLED MONOCLONAL ANTIBODIES

Investigators: M.K. Woo, P. O'Brien and R. Reed

This project is part of an ongoing plan to develop a reliable system for the dosimetry of radiolabelled monoclonal antibodies. Initial studies consisted of measurements in solutions of radioactive isotopes using either thermoluminescent dosimeters or ionization chambers. Calibrations were performed in air using the chosen isotope, usually technecium-99m. The absorbed dose measurements are compared with values calculated using the medical internal radiation dose protocol, a scheme based upon computer modelling. The initial results indicate that perturbation effects may have a significant impact on measured doses.

VIDEO-BASED FILM DOSIMETRY

Investigators: P. O'Brien and S. Bibla

Following the design work for a digital film-dosimetry system carried out by R. Barnett, we tested the video-based system and calibrated it to convert film densities to absorbed dose. Hardware consisted of a lenearly responding vidicon camera, a high-quality illuminator and a frame grabber in an IBM-386 computer.

Analysis was done using software written at our Centre. The characteristics of the system include spatial resolution of 1.5 mm, a maximum exposed film size of 15x20 cm and an uncertainty in relative absorbed dose of 2.5%.

STEREOTACTIC RADIOSURGERY

Investigators: C. Young, M. Schwartz, P. O'Brien, P. Davey and B. Gillies

Development of our stereotactic radiosurgery facility continued in 1989. Protocols for the treatment of arteriovenous malformations and for brain metastases have been written and are being followed. Improvements to the treatment hardware include an encoder-based readout system to display stretcher co-ordinates. After set-up and during treatment, this display can be monitored to ensure the accuracy of target positioning.

Division of Epidemiology and Statistics, Toronto

EPIDEMIOLOGY RESEARCH UNIT*

E.A. CLARKE**, G. DARLINGTON†, E. HOLOWATY††,
N. KREIGER‡, L.D. MARRETT‡‡ and J. McLAUGHLIN§
Toronto, Ontario

Since 1978, the Epidemiology Research Unit of the Division of Epidemiology and Statistics has been affiliated with the Department of Preventive Medicine and Biostatistics at the University of Toronto. The Unit was established to conduct analyses using the cancer data-bases of the OCTRF, to assess the quality of these data, to provide cancer research workers with epidemiological and biostatistical assistance, to conduct or support cancer research projects, and to provide information on cancer to the general public and the scientific community.

Members of the Unit, holding academic appointments at the University, are Drs. E.A. Clarke, G. Darlington, E. Holowaty, N. Kreiger, L. Marrett and J. McLaughlin. Other staff members are I. Fan, J. Fleury, S. Hilditch, D. Nishri, K. Rentner, T. Sardinha and M. Swift. Additional Unit members who are supported by externally funded research projects are: D. Bijelic, S. Chin Cheong, K. Easun and S. Ferrier.

---

*Project 381.

**Director, Division of Epidemiology and Statistics, Ontario Cancer Treatment and Research Foundation, Vice President OCTRF; and Associate Professor in the Department of Preventive Medicine and Biostatistics, University of Toronto.

†Biostatistician, Division of Epidemiology and Statistics, OCTRF; and Lecturer in the Department of Preventive Medicine and Biostatistics, U of T.

††Head, Cancer Registration Unit, Division of Epidemiology and Statistics, OCTRF; and Assistant Professor in the Department of Preventive Medicine and Biostatistics, U of T.

‡Head, Statistics Unit, Division of Epidemiology and Statistics, OCTRF; and Assistant Professor in the Department of Preventive Medicine and Biostatistics, U of T.

‡‡Director, OCTRF Epidemiology Research Unit; and Associate Professor in the Department of Preventive Medicine and Biostatistics, U of T.

§Senior Epidemiologist, Division of Epidemiology and Statistics, OCTRF; and Assistant Professor in the Department of Preventive Medicine and Biostatistics, U of T.

The Unit provides the site for much of the externally funded research of the Division of Epidemiology and Statistics. Recently, etiologic case-control studies of renal-cell carcinoma, thyroid cancer, bone cancer, malignant germ cell cancer, and lymphoma and soft-tissue sarcoma have been conducted here. Many of these studies used the Ontario Cancer Registry to identify cases and involved collaboration with other investigators and agencies.

Staff of the Unit have participated in many projects based on the Ontario Cancer Registry, such as: survival analyses for various types of cancer; preparation of a cancer mortality atlas for Ontario; investigation of the risk of congenital anomalies in the offspring of cancer patients; review of the quality of data in the Registry; and investigation into the identification of native peoples in the Registry to permit the study of their cancer patterns.

In addition, analyses are being carried out using data collected during case-control studies conducted by senior Epidemiology Research Unit staff in past years. These include examination of the association between cigarette smoking and endometrial neoplasia; the risk of malignant melanoma associated with constitutional factors; and the effect of follow-up procedures on estimates of relative risk in case-control studies based on postal questionnaires.

Our staff have developed microcomputer software to display the data being generated by the Ontario Cancer Registry, such as graphs of time trends in the incidence or mortality of various types of cancer, maps of cancer mortality by county, and calculation of rates for specified subgroups of patients. These derivatives have been useful in investigating the patterns of cancer in Ontario.

Staff of the Research Unit organized the OCTRF's 1990 Cancer Epidemiology Seminar. This year's themes were: "Investigation of Clusters" with talks by Drs. N. Kreiger of OCTRF, A. Stark of the New York State Department of Health, and J. Heller of the Ontario Industrial Disease Standards Panel; and "Radon and Cancer" with presentations by Drs. K. L'Abbe of the Ontario Industrial Disease Standards Panel and R. Eaton of Health and Welfare Canada. Dr. John McLaughlin of OCTRF provided an overview of cancer trends in Ontario.

Finally, those with academic appointments have been involved in teaching epidemiology and biostatistics to undergraduate medical students and graduate students (M.Sc. and Ph.D. candidates).

This project is supported by the OCTRF.

ADDITIONAL INVESTIGATIONS

Dr. E.A. Clarke, Director, Division of Epidemiology and Statistics, and Vice-President OCTRF reports on the following studies:

CHILDHOOD LEUKEMIA AROUND NUCLEAR FACILITIES

Investigators: E.A. Clarke, J.R. McLaughlin and T.W. Anderson

This study determined whether clusters of childhood leukemia exist in children born to mothers residing in the vicinity of major nuclear facilities in Canada, the majority of which are in Ontario. It was initiated in response to findings in the U.K. of childhood leukemia clusters near two nuclear installations.

Children, aged 0-14 years, who died from or developed leukemia were identified from both the mortality file (1950-1987) and the incidence file (1964-1986) of the Ontario Cancer Registry. The birth certificates of these children were used to determine the mother's residence at the time of the child's birth. The annual number of live births, by mothers' residence in the five counties of interest, were obtained from Ontario Vital Statistics. The rate of leukemia in relation to live births was calculated for each area and compared with the provincial rate. The preliminary analysis indicated that slightly more leukemia occurred than was expected; however, even with the long period covered by this study, there were few cases and the excess could have been due to chance alone.

This project is funded by the Atomic Energy Control Board.

CARDIAC CATHETERIZATION AND THE RISK OF CANCER: A FOLLOW-UP STUDY

Investigators: N. Kreiger, J. McLaughlin, S. Hilditch and E.A. Clarke

Children with congenital heart disease, who undergo cardiac catheterization, may receive significant radiation exposure during multiple chest fluoroscopies. Compared to the general population, this study evaluates the risk of cancer in later life among those with childhood exposure to cardiac catheterization.

Patients, who were catheterized at the Hospital for Sick Children (HSC) in Toronto between 1950 and 1965, were linked with the Ontario Cancer Registry incidence file (1964-1985) and with the Ontario death file (1950-1985). Rates of cancer in these patients were compared with those of the general population.

A total of 7 cancer deaths were observed (0) compared with 5.7 expected (E), for a mortality ratio (O/E) of 1.2, which was not significantly different from 1.0. In the analysis of cancer incidence, 13 definite links were detected, compared with 17.3 expected (O/E = 0.75). It is concluded that, in general, there has been no statistically significant excess of cancer among the cohort.

This project is funded by the Atomic Energy Control Board.

OCCUPATIONAL EXPOSURE OF FATHERS TO IONIZING RADIATION AND THE RISK OF LEUKEMIA IN OFFSPRING—A CASE-CONTROL STUDY

Investigators: J.R. McLaughlin, E.A. Clarke, T.W. Anderson

The primary objective of this case-control study is to examine the association between childhood leukemia and the cumulative occupational exposure of fathers to ionizing radiation at the time of a child's conception. The study focuses on the effect of exposures received while at work in the nuclear industry, especially in the year before conception.

Cases are children (aged 0-14 years) who died of or were diagnosed with leukemia and were born to mothers who, at the time of the child's birth, resided in the vicinity of a nuclear facility. Cases were identified from the Ontario Cancer Registry. Control children have not developed leukemia and are matched to cases in terms of date of birth and mother's residence at the time of birth.

The National Dose Registry (NDR), which is maintained by the Bureau of Radiation and Medical Devices of the Department of National Health and Welfare, is being used as the primary source of radiation dose information for occupationally exposed workers in Ontario. Record linkage is underway to obtain the relevant radiation dose information from the NDR.

This project is funded by the Atomic Energy Control Board.

RADIATION EXPOSURE AND BONE CANCER

Investigators: N. Kreiger, M. Finkelstein, P. Beck and A. Lye

This population-based case-control study will provide information on the risk of bone cancer associated with radium content in drinking water. It also will address the risks associated with other factors, including prenatal and early childhood exposures. The study has two parts: one will concentrate on investigating the association between bone cancer and radium in drinking water; the other will examine the effects of several other potential risk factors. Cases comprise patients 25 years of age or younger with bone cancer in the Province of Ontario. They have been identified through reports submitted to the Ontario Cancer Registry (OCR) between the years 1964 and 1988. There are two control groups: one identified through OCR records, the other selected through random digit dialling of the telephone. Controls are of the same age and sex as the cases.

Mothers of subjects given this diagnosis before 1980 have been asked to complete a brief questionnaire concerning their residence history; mothers of subjects diagnosed since 1980 have completed a more detailed questionnaire regarding the subjects' prenatal and childhood exposures. With the knowledge of the subjects' mothers, water samples have been taken at their previous residences. Statistical analysis will be done to ascertain differences between cases and controls.

Data collection is nearly complete. Coding, editing of questionnaires, and data entry are underway. Analysis will follow.

This project is funded by the Ontario Ministry of Health.

STEROID-RECEPTOR CONTENT AND THE EPIDEMIOLOGY OF BREAST CANCER

Investigators: N. Kreiger, W. King and E.A. Clarke

Evidence that the prognosis of breast cancer patients is associated with tumor, estrogen-receptor (ER) and progesterone-receptor (PR) status has provoked interest in the epidemiology of breast cancer in relation to steroid receptors. This case-control study looks at known and suspect risk factors for breast cancer according to tumor ER status and PR status. The project is part of a multicentre collaborative study of primary breast cancer.

The data included 607 cases and 1214 controls matched for age and residence. Of 528 cases with steroid-receptor information, 67% had ER positive (ER+) tumors and 55% had PR positive (PR+) tumors. Odds ratios for ER+ and ER negative (ER-) breast cancer were similar with respect to menopausal status, age at menarche, history of cystic breast disease and Quetelet index. Family history of breast cancer was a stronger risk factor for ER- than for ER+ breast cancer and the odds ratios for number of births were suggestive of a different effect.

While ER and PR status were highly correlated, there were some differences in their associations with risk factors. Odds ratios for PR+ and PR- breast cancer differed for number of births and were suggestive of differences with respect to menopausal status, Quetelet index, and family history of breast cancer. These findings do not suggest different causal pathways for ER+ and ER- breast cancer, however, they do indicate that PR status may play a role in the etiology of breast cancer.

This project is funded, in part, by the Ontario Ministry of Health.

THE ETIOLOGY OF RENAL-CELL CARCINOMA IN ONTARIO

Investigators: L.D. Marrett, N. Kreiger, L. Dodds and S. Hilditch

In 1986, we began a case-control study of the etiology of renal cell carcinoma in Ontario. Patients with newly diagnosed kidney cancer for the period 1986 and 1987 were sent a brief questionnaire requesting information on smoking, dietary habits, occupational exposures, use of analgesic and diuretic medications, and basic demographics. We sent the same questionnaire to a random sample of the population selected from enumeration records held by the Ontario Ministry of Revenue. Nearly 90% of cases and 74% of population controls responded—a high rate of response for this type of survey.

Data collection is completed (513 cases and 1369 controls), and analysis is ongoing. As anticipated, cigarette smoking, obesity and use of diuretic medications increase the risk of renal-cell carcinoma. We hope that ultimately risk-factor modification will reduce the incidence of renal-cell carcinoma.

This project is funded by the Ontario Ministry of Health.

THE ETIOLOGY OF MALIGNANT GERM CELL TUMORS

Investigators: L.D. Marrett and H. Weir

Usually malignant germ cell tumors (MGCT) develop in the testis but also can appear in the ovary and at extragonadal sites, although less frequently. Most testicular cancers (TC) in males and ovarian tumors in females under age 15 are of germ cell origin. In recent years, incidence rates for TC have been rising in Ontario and elsewhere. Also the childhood incidence of ovarian cancer and MGCT (of all sites) appears to be increasing for reasons that as yet are unknown.

This study is investigating the etiology of MGCT in Ontario. Cases, which are being identified through the Ontario Cancer Registry, constitute all Ontario residents diagnosed with MGCT between 1986 and 1989, age 59 or less. Age and sex stratum-matched controls have been selected from the assessment rolls of the Ministry of Revenue. Relevant exposure information is being collected through questionnaires sent to subjects and/or their mothers.

Some have suggested that the totipotentiality of germ cells in TC changes with age. This fact may have implications for the study of MGCT of all sites: for example, disease state according to histologic groupings, which correspond to the changing totipotentiality of the germ cells, may elucidate etiologic risk factors specific to these histologic subgroups. This study includes a slide review to achieve a uniform classification of all tumors. In addition, we will describe the detailed age, sex, site and histology distribution of these tumors in the population.

A collaborative analysis is also proposed with centres in Denmark and British Columbia/Alberta where similar studies on TC have been done recently or are being done. Descriptive analysis correlating exposure variables in the population with incidence of disease, where disease rates vary substantially, may provide insight into the international variability of TC incidence rate.

We expect to collect data on about 700 cases, 1300 controls and 1200 mothers. Response rates to date have been gratifyingly high.

This project is funded by the Ontario Ministry of Health.

CONGENITAL ANOMALIES IN THE OFFSPRING OF CANCER SURVIVORS

Investigators: L.D. Marrett and G.J. Sherman

In many cancers of childhood and young adulthood, long-term survival and cure are now possible largely as a result of chemotherapy and radiation. While some late complications of cancer therapy have been recognized, little is known about the well being of the offspring of cancer survivors.

We are conducting a case-control study to determine whether the offspring of former cancer patients are at an increased risk of congenital anomalies and, specifically, whether preconception treatment (radiation and chemotherapy) is responsible for such an increase. Cases are defined as the parents of Ontario liveborn children recorded in the Canadian Congenital Anomalies Surveillance System (CCASS) between 1979 and 1986, and controls are parents of a random sample of children not registered in CCASS, selected from Ontario livebirth certificates.

Cancer diagnoses made before the index birth and between 1964 and 1986 have been identified for both case and control parents through computer linkage with the Ontario Cancer Registry. Treatment details have been collected from records of the regional cancer centres, hospitals, and physicians for all those with cancer.

Relative risk associated with a history of cancer and type of therapy will be estimated. The results of this study may contribute information concerning potential adverse effects of cancer therapy in long-term cancer survivors.

This project is funded by the Ontario Ministry of Health.

GEOGRAPHIC VARIATION IN ONTARIO CANCER RATES

Investigators: S.D. Walter, L.D. Marrett, S.M. Taylor, J.D. Drake, J.A. Davies and M.V. Hayes

This study examines the spatial variation in incidence rates for the major cancer sites in Ontario, using sophisticated statistical techniques. County-level, cancer-incidence data from the Ontario Cancer Registry (OCR) for two time periods, namely 1964-1975 and 1976-1986, provide the basis for this study. Persistence of spatial patterns between the two time periods is being investigated.

As part of this project, we are evaluating the quality of residence information stored in the OCR. In addition, for each county, we are estimating the number of cases which have not been ascertained by the OCR or which have no residence information; also we will examine the geographic patterns of "missingness".

An additional objective of the study is to investigate the feasibility of conducting a formal ecologic analysis relating cancer rates to environmental variables such as water quality, air contamination, and degree of urbanization and industrialization.

Spatial and quality of data analyses have been completed for several major cancer sites, and results are being studied. We have completed investigation into the existence, quality, and availability of environmental databases for ecologic studies.

This project is funded by the Ontario Ministry of Health.

LEUKEMIA FOLLOWING RADIOTHERAPY FOR UTERINE CORPUS CANCER

Investigators: E.J. Holowaty and P. Toogood

This population-based, case-control study will provide information on the risk of leukemia among Ontario women treated with radiation for uterine corpus cancer (UCC) Of particular importance will be the determination of the relationship between dose of radiation delivered to active marrow elements and subsequent risk of leukemia.

This study was conducted in collaboration with the Radiation Epidemiology Branch of the National Cancer Institute, Bethesda, Maryland, along with cancer registries in United States and Scandinavia. Ontario women diagnosed with uterine corpus cancer during the period 1964 to 1985, who were registered in the Ontario Cancer Registry and who survived at least 12 months were eligible. Cases were subjects who had been diagnosed with leukemia at least 12 months after UCC diagnosis. Controls were subjects with UCC who did not have a second primary - they were matched to each case (4:1) based on date of diagnosis of UCC, age, and duration of leukemia-free survival. Relevant study information was abstracted from records in hospitals and regional Cancer Centres. Radiation dosimetry was conducted at the M.D. Anderson Hospital in Houston, Texas.

Of approximately 17,000 Ontario women who were eligible members of the inception cohort, 35 eligible cases were identified and 120 controls were matched. Approximately 71% of cases (25/35) and 57% of controls (68/120) received some radiotherapy for uterine corpus cancer. Of these, most received brachytherapy only (79%) while most of the remainder received both external beam and brachytherapy (18%). Preliminary analysis, using conditional logistic regression, has revealed a relative risk of leukemia of 1.6 (90% CL: 1–2.2) for Ontario subjects who ever received radiotherapy for UCC. For all leukemias other than chromic lymphocytic leukemia, the relative risk was higher (O.R.=1.9, 90% CL:0.8–4.3). Analysis will continue through the spring of 1991 and will include estimation of the relationship between dose of radiation to the active bone marrow and risk of leukemia.

The findings support an association between radiation therapy for UCC and subsequent risk of leukemia.

This project is funded by the National Cancer Institute, Bethesda, Maryland.

SECOND CANCERS FOLLOWING TREATMENT FOR UTERINE CORPUS CANCER

Investigators: E.J. Holowaty and P. Toogood

This population-based cohort study is to estimate the risk of all second cancers following treatment for uterine corpus cancer (UCC) This study was conducted in collaboration with the Radiation Epidemiology Branch of the National Cancer Institute, Bethesda, Maryland, along with cancer registries in the United States and Scandinavia. Observed and expected numbers of second primary cancers were evaluated by time since diagnosis of uterine corpus cancer (UCC) age at initial diagnosis, and histologic type of UCC. All Ontario women diagnosed with UCC between 1964 and 1987 and registered in the Ontario Cancer Registry, and without a prior malignancy, were eligible. Most of the diagnostic information for this study was readily available from the Ontario Cancer Registry. Additional information was collected from hospitals and OCTRF Regional Cancer Centres.

Approximately 17,000 subjects were confirmed eligible for this study. A total of 1236 second primaries were identified for these subjects. Expected numbers of second primaries were calculated using person-years at risk, with cancer rates derived from the Ontario Cancer Registry. Of approximately 30 cancer sites examined, risks were elevated and statistically significant ($p<0.05$) for four sites: leukemia (relative risk=1.6); breast (RR=1.2); bladder (RR=1.4); and connective tissue (RR=2.8). For all sites combined, the risk was also elevated (RR=1.2) and statistically significant. Analysis is planned of the latency in onset for these second cancers in relation to time of treatment for UCC.

This study provides evidence for an increased risk of certain cancers following UCC. Because of the pattern of latency for some of these second cancers in relation to initial treatment for UCC, it is more likely they are related to UCC treatment, than to risk factors in common with UCC. Future case-control studies may shed additional light on the etiology of these second cancers.

This project is funded by the National Cancer Institute, Bethesda, Maryland.

University of Toronto

THE RETINOBLASTOMA (RB) GENE IN HUMAN CANCER*

B.L. GALLIE**, *Toronto, Ontario*

Study of RB, a rare tumor of infant retina, has revealed mechanisms fundamental to cancer induction, and has demonstrated the role of tumor-suppressor genes in human cancer. The Toronto Retinoblastoma Group continues to study RB in four major research areas.

1. Cloning of RB gene (*RB1*) lead to the discovery that the RB protein (pRB) is important in the control of cell division. Since pRB may act by altering expression of other genes which in turn signal cells to divide, we are characterizing the molecules which interact with the pRB. Mechanisms controlling pRB expression and modification are being studied by constructing specific mutations, assayed in whole cells[1]. In both RB and breast-tumor cells deleted for pRB, which have been reconstituted by the replacement of a normal RB gene, we have observed little effect on cell growth, but differentiation of the reconstituted cells is altered, and new proteins are induced.
2. Although mutations in *RB1* affect every cell of the body, only certain tissues, especially retina, develop cancer. To characterize the unique susceptibility of the developing retina, we are using retroviruses to identify genes which characterize the cell of origin of RB. The markers obtained will permit isolation of these cells for characterization of the unique spectrum of cellular proteins which are interacting with the pRB, in comparison to cells of other tissues which are not susceptible to malignancy in the absence of pRB.
3. We have identified the germ line *RB1* mutation in families[2]. Since each family has a unique mutation, an efficient screening procedure is being developed. Once a family's *RB1* mutation is identified, a screening procedure is devised for family members. Prenatal and pre-

---

* RA-202-1.

** OCTRF Research Associate; and Professor of Ophthalmology, Pediatrics, and Medical Genetics, University of Toronto.

malignant diagnosis can be accomplished, permitting vision to be saved in children who otherwise would lose one or both eyes.

4. In collaboration with Dr. Helen Chan, a new approach to treatment of intraocular RB tumors is being studied. Chemotherapy allows us to treat larger tumors with cryotherapy. We now are proposing a protocol to include manipulation of the multidrug resistance protein to control intraocular RB.

REFERENCES

1. Hamel PA, Cohen BL, Sorce LM, Gallie BL, Phillips RA: Hyperphosphorylation of the retinoblastoma gene product is determined by domains outside the SV40 large-T-binding regions. *Mol Cell Biol* 1990; **10**: 6586.
2. Dunn JM, Phillips RA, Zhu X, Becker AJ, Gallie BL: Mutations in the RB1 gene and their effects on transcription. *Mol Cell Biol* 1989; **9**: 4594.

RELATIONSHIPS OF PHEOMELANINS AND PHOTOSENSITIZERS TO SKIN CANCER*

H.F. HABERMAN** and I.A. MENON†, *Toronto, Ontario*

Individuals with pheomelanin in the hair and possibly in the skin have higher susceptibility to ultraviolet (UV)-induced skin cancers. We are continuing our studies on the biological effects of pheomelanin and UV radiation. Photosensitization of pheomelanin induces peroxidation of lipids, indicating that membrane lipids may be one of the targets of UV in pheomelanin-containing skin.

We investigated the reactive species involved in the photosensitization of various porphyrin derivatives present in porphyrias and those used in the treatment of malignant diseases. Singlet oxygen was the primary product of such photosensitization. However in the presence of reducing agents such as cysteine, glutathione, ascorbic acid, this process produces considerable amounts of superoxide, hydrogen peroxide and hydroxyl radical. It is the product of these reactive species which produce the biological effects associated with photosensitization.

We have continued our studies on the mechanisms of acute inflammatory reactions produced by psoralen, using the rabbit model we developed. Various manifestations of the inflammatory reactions are mediated by different biological mediators; for instance, the increase in vascular permeability and accumulation of leucocytes were mediated by histamine. However histamine did not produce erythema associated with this reaction.

---

* RA-203.

** OCTRF Research Associate; Head of Dermatology, The Toronto Hospital, Toronto Western Division; and Associate Professor of Medicine, University of Toronto.

† Assistant Professor of Medicine, and Ophthalmology, U of T.

HORMONE RECEPTOR MECHANISMS IN THE DEVELOPMENT AND TREATMENT OF PROSTATIC NEOPLASIA*

G.E. MOBBS**, *Toronto, Ontario*

Although most advanced prostatic cancers respond initially to treatments designed to deprive the tumor of androgen, resistance develops eventually resulting in tumor progression. There is little effective treatment for prostatic carcinoma which has reached this stage. We have used an experimental rat prostatic carcinoma to investigate a new form of hormonal treatment that is not based on androgen sensitivity.

The R3327HI rat prostatic carcinoma is derived from the androgen-insensitive subpopulation of the R3327H (Dunning) tumor by passage of the latter in castrated animals and is considered to be a model for human prostatic carcinoma, which has become resistant to androgen deprivation. Earlier, we showed that the R3327HI tumor contains a significant concentration of progesterone receptor (PgR) and that this is increased approximately 10-fold by treatment of the host animal with diethylstilbestrol (DES). The antiprogestin RU486 inhibits the growth of a number of tumor-cell lines and solid tumors which contain significant concentrations of PgR. Some workers have suggested that growth suppression may be due to a PgR-mediated cytotoxic effect. For this reason, we set out to investigate the possibility that RU486 would suppress the growth of the R3327HI tumor, especially in DES-treated animals. We treated tumor-bearing animals for 2 or 8 weeks with RU486 alone, DES alone, combine RU+DES or a vehicle. Growth was assessed by changes in tumor diameter, [^{3}H]thymidine uptake and histopathology. Also we measured estrogen and progesterone receptor content. Tumor growth was not affected by RU486 or DES alone, but was suppressed significantly by combined treatment ($p<0.05$ at 8 weeks). This suppression was accompanied by atrophy of the glandular epithelium. RU486 treatment alone suppressed the PgR content of the tumors ($p<0.02$ vs controls), but concurrent administration of DES maintained this at control levels, supporting the hypothesis that growth suppression may be brought about by a PgR-mediated mechanism. These data suggest that it may be possible to treat at least some androgen-sensitive prostatic carcinomas by a new form of hormonal treatment.

This project is supported by a grant from the National Cancer Institute of Canada.

---

*RA-205-1.

**OCTRF Research Associate; and Associate Professor of Surgery (Research), University of Toronto.

EPIDEMIOLOGY AND STATISTICS

DIVISION OF EPIDEMIOLOGY AND STATISTICS

HEAD OFFICE

Director, Division of Epidemiology and Statistics and Vice-President OCTRF:
E.A. Clarke, M.B.,B.S.

Cancer Registration Unit:
D. Dale, B.A.Sc.
E.J. Holowaty, M.D.
F. Lu, M.D.
W. Muscatello, C.C.H.R.A.(A)

Provincial Programs Unit:
M. Nefsky, M.Sc.
M. Nemes, C.C.H.R.A.(A)

Senior Epidemiologist:
J. McLaughlin, Ph.D.

Statistics Unit:
G. Darlington, Ph.D
G. Fehringer, M.Sc.
G. Hunter, S.R.N.
W. King, M.Sc.
N. Kreiger, Ph.D.
M. Sloan, M.Sc.
P. Toogood, B.Sc.
H. Weir, M.Sc.

Epidemiology Research Unit:
I. Fan, B.A.
J. Fleury, B.Sc.
S. Hilditch, M.S.W.
L.D. Marrett, Ph.D.
D. Nishri, M.Sc.
K. Rentner, B.Math.
M. Swift, M.Sc.

Since May 1989, Dr. E.A. Clarke has been seconded to the Ministry of Health as cancer co-ordinator. Her commitment of 50% increased to 60% in 1990/91. A management committee was established to deal with the operational issues. The committee, consisting of Drs. Holowaty, Kreiger, Marrett, McLauglin and Mrs. Nefsky with the support of Mrs. Erochko and Mrs. Holman, meets regularly to review the issues facing the Division and to make decisions with the chairman of the committee.

The Division continues to play an active role in cancer-control activities, providing information not only on incidence and mortality in Ontario but, this year, on survival over time for all cancer patients in Ontario. Information is continually disseminated to government, health-care planners, research workers and others within the province and elsewhere.

In 1990, the Cancer Registration Unit started a redevelopment and growth phase in order to meet its strategic objectives. We have added additional staff for coding and data entry—J. Freud, A. Gonsalves, C. Lauzon, P. Leishman, M. McMillan, M. Rahnema and a coding supervisor—W. Muscatello. The staff have the responsibility for producing a timely and high-quality pathology file. In addition, in 1991, we will examine the feasibility of actively following up cancer cases identified solely through hospital separation abstracts. These cases amount to about 15 to 20% of total annual incidence.

Dr. F. Lu is now our Manager of Development, a position which was made permanent. With the assistance of a new research assistant, N. Chong, Dr. Lu will address the redevelopment of the case resolution system and will co-ordinate the development of a comprehensive, scientific, quality-control program for the Registry.

The Ontario Cancer Registry Information System (OCRIS) project, which aims to redevelop the Registry data base, is now well underway. Phase I included the design and implementation of data capture systems. The first on-line system for pathology reports was released in May 1990. We expect the remaining data-capture systems, for hospital separations, regional cancer centre registrations and death certificates, to be completed and released in 1991. As part of this major redevelopment, we will review and revise all of the computerized editing systems.

In 1990, Mrs. M. Sloan was recruited as biostatistician in the Statistics Unit and Mr. G. Hyman was recruited to serve as systems analyst for the Division.

The Statistics Unit continued to provide statistical information derived from the Ontario Cancer Registry in response to requests. The Statistics Unit invested in a "desk top" publishing system to prepare publications for the Division. These reports will include analyses of cancer incidence and mortality, a cancer atlas for the province and studies on cancer projections and survival. The Epidemiology Research Unit continues to provide a vital link with the University of Toronto and a base for field studies.

In January 1991, Dr. V. Goel will join the Division as head of the newly created Evaluation Unit, which will be responsible for developing and implementing the evaluation of program of cancer prevention, early detection and treatment.

Dr. V.C. Nguyen, epidemiologist with the Northeastern Ontario Regional Cancer Centre, continues to respond to requests for statistical information on northeastern Ontario residents and to participate in analytical studies with other staff in the Division.

In addition to in-house studies, staff of the Division collaborated in a number of research projects with external agencies such as Statistics Canada, the Atomic Energy Control Board, the International Agency for Research on Cancer and the National Cancer Institute in United States.

The Annual Seminar in Cancer Epidemiology, organized by the Epidemiology Research Unit, was held in April 1990. The seminar included an overview of cancer trends, provided by Dr. J. McLaughlin, a session on the investigation of clusters, presented by Drs. N. Kreiger, A. Stark and J. Heller, and a session on the effect of radon by Drs. K. L'Abbe and R. Eaton.

In June, all staff of the Division attended a one-day retreat at the MacLean House in Toronto. In the morning, a time-management seminar was held and, in the afternoon, small working groups examined the problems faced by a hypothetical department similar to the Division.

In November, the Division organized the visit of Dr. Denis Burkitt to Toronto. Dr. Burkitt, renowned for his discoveries of Burkitt's lymphoma and the role of dietary fiber in colon cancer, presented the Gordon Richards Memorial Lecture at Princess Margaret Hospital, entitled "Winning the War on Cancer". In addition, Dr. Burkitt presented a lecture at the University of Toronto, entitled "A Healthy Western Lifestyle: Lessons from Africa" and met with representatives of the Ministry of Health, the Department of Preventive Medicine and the City of Toronto Health Department.

In 1990, the Division hosted two fellows from India, who were sponsored by the International Agency for Research on Cancer, to undertake research in cancer epidemiology using data from the Ontario Cancer Registry.

Following this summary of the activities of the Division, we present the most recent data concerning cancer incidence, mortality and treatment in Ontario.

E.A. Clarke, M.B., B.S.
Director, Division of Epidemiology and Statistics, and
Vice-President OCTRF

CANCER INCIDENCE, MORTALITY AND TREATMENT IN ONTARIO

The Division of Epidemiology and Statistics is responsible for the reporting of cases and the recording and compilation of data, both of which are part of the mandate of the Foundation under the Cancer Act. In pursuit of this objective, the Foundation has maintained and improved a uniform case-recording system, which was adopted by the OCTRF Regional Cancer Centres in 1947 and by the Ontario Cancer Institute incorporating the Princess Margaret Hospital (OCI/PMH) in 1957. The data from the OCTRF Regional Cancer Centres and the OCI/PMH are in machine-readable form from 1960 onwards. In addition to these records, the Foundation's computerized cancer-data base contains: individual records on residents of Ontario who died from cancer since 1950; tabulations of deaths by sex, five-year age groups, and type of cancer from 1931 to 1990; individual records of hospital separations describing patients with cancer from 1964 to 1989; and pathology reports on biopsy specimens with cancer from 1972 to 1989. The total volume of the data base, presently almost 6 million source records, including more than 1.6 million source records on all deaths, provides the Division with a unique resource for descriptive cancer epidemiology and allows the Division to assist other cancer research workers in their epidemiologic investigations.

CANCER INCIDENCE AND MORTALITY

The Ontario Cancer Registry

The Ontario Cancer Registry now has 25 years of incidence data for the province describing 645,000 incident cases of cancer diagnosed in residents of Ontario between 1964 and 1988.

The Ontario Cancer Registry employs a unique system of registration, based on computerized record linkage of cancer records collected routinely for other purposes and provided to the Foundation. The Registry receives about 300,000 such records annually. The following province-wide data are routinely forwarded to the Registry:

1. Hospital separations with a mention of cancer collected by the Hospital Medical Records Institute (HMRI) and supplied by the Ontario Ministry of Health; 135,000 computerized records per year.
2. Pathology reports with a mention of cancer submitted voluntarily by hospital pathology laboratories; about 67,000 paper records per year.

3. Reports on patients referred to the OCTRF Regional Cancer Centres and the OCI/PMH; 22,000 computerized records per year.
4. Deaths from all causes supplied by the Registrar General of Ontario; 70,000 computerized records per year.

Once source files are preprocessed, cancer incidence data are created in two major phases. First, the source files are linked in a sequential fashion to bring together all records pertaining to an individual. To link the large volume of data, the Foundation staff have developed a sophisticated, computerized, probabilistic, record-linkage system, based on the Generalized Iterative Record Linkage System (GIRLS), designed by Statistics Canada in conjunction with the Epidemiology Unit of the National Cancer Institute of Canada. A set of computerized rules called "case resolution" is then applied to the linked records to determine site of disease, histology, and date and method of diagnosis.

The generation of cancer incidence data for Ontario is a joint effort of the Division of Epidemiology and Statistics and Information Systems who, together, have developed these systems of record linkage and case resolution.

All incidence data presented here are classified according to the International Classification of Diseases, Ninth Revision (ICD9). Although the Registry had coded cancer sites according to the Eighth Revision of the ICD between 1964 and 1978, all records now have been converted to ICD9.

Cancer Incidence and Mortality, 1988

This year, as a result of our efforts to improve the efficiency of the Registry's operation, the frequencies and rates of cancer incidence for 1988, presented in Tables I to IV, are almost complete. Since these data are more complete than those published in previous editions of *Cancer in Ontario* for the years prior to 1987, we would caution the reader against making comparisons against making comparisons over time from this source. Available upon request is more complete information describing cancer incidence over the interval 1964 to 1988, including incidence data for smaller geographic areas in the Province (e.g. county) and at the four-digit ICD9 site level. Normally such data can be provided free of charge, within six to eight weeks, following receipt of a written request. We anticipate that provisional incidence data for 1989 will be available by March 1991.

Tables I and II give the frequencies by 5-year age group for each cancer site or group of sites, for males and females respectively, for 1988. The far right-hand column gives rank order to identify sites of most frequent occurrence. The 10 most common sites, in terms of their sex-specific incidence frequencies, are shown in Fig. 1 with cancer mortality data for 1988.

Tables III and IV present incidence and mortality rates by age group and site, for males and females respectively, for 1988. In these two tables, the rates for 15-year age groups and for all ages are age-adjusted, using the world standard population shown in Table VII.

The method of direct age-adjustment used here is described by Muir *et al* in *Cancer Incidence in Five Continents*, vol. 5. Rates in the tables have been "age-adjusted" to assist comparisons between the different areas in the world. Age adjustment allows us to account for differences caused solely by differences in age distribution in these areas. The rates in Tables III and IV can be compared with any other rates covering the same age span and using the same standard population for adjustment.

The "cumulative risk" (CR), shown in the final column of Tables III and IV, is described in detail in *Cancer Incidence in Five Continents*. Expressed per 100, it is a reasonable approximation to the risk (to age 74) of being diagnosed with, or dying of, the given cancer. Thus, if the current age-specific rates for female lung cancer were to remain unchanged throughout her life, a female born in 1988 would have about a 3% chance of being diagnosed with lung cancer by age 74. Of course, if age-specific rates continue to rise, the cumulative risk will increase also.

Cancer Mortality, 1989

The most current cancer mortality data are for 1989; these were provided by the Office of the Registrar General of Ontario. Figs. 2 and 3 show the frequencies of death due to malignant neoplasms of all types, relative to other major groups of causes of death among males and females. Tables V and VI give the numbers of cancer deaths by age group at death and site; the same format and groupings are used in Tables I and II for cancer incidence.

Populations

Table VII shows sex- and age-specific population data for Ontario for the years 1988 and 1989 and for the "world standard". This table provides the 1988 and the 1989 Ontario population (post-censal estimates) for those who wish to calculate age-specific cancer incidence and mortality rates from data given in the previous sections. The world population is an artificial standard, frequently used in the calculation of age-adjusted rates. The Ontario population data are provided by Statistics Canada and the world population is taken from *Cancer Incidence in Five Continents*.

CANCER TREATMENT

Hospital Caseload

During the fiscal year 1988-89, active and rehabilitation hospitals in Ontario reported 76,012 separations (discharges and deaths), in which the primary diagnosis was cancer. These accounted for 5.8% of all hospital separations and 1,108,249 days of hospital care. The average length of stay for cancer patients declined from 16.9 days in 1972 to 14.6 days in 1988-89*.

New Cancer Registrations

In the last decade (1980-1989), the number of new cases (a patient presenting with a case of cancer not previously registered at any centre) registered at the OCTRF Regional Cancer Centres and the OCI/PMH has increased by 42.4% from 16,864 to 24,021 (Table VIII). However, for the first time in more than 20 years, there has not been an increase in the last year. Examination of the last two columns of in Table VIII indicates that this was due to a large extent to the reduction in numbers of new cases seen at the Princess Margaret Hospital attributable to the shortage of radiation resources (both in machines and personnel) in the province.

The distribution by centre of the numbers of *in situ* lesions, neoplasms of uncertain behaviour and multiple skin cancers is shown at the foot of Table IX.

In Table IX, for 1989, the major sites of newly registered cancers at the OCTRF Regional Cancer Centres were lung, bronchus and trachea (15.4%), and breast (19.2%), followed by non-melanoma of the skin (8.2%). Of the 22,319 cancers seen for the first time at one of the OCTRF Regional Cancer Centres or the OCI/PMH, 16.3% were seen in Hamilton, 5.9% in Kingston, 14% in London, 14.4% in Ottawa, 2.1% in Sudbury, 2.9% in Thunder Bay, 15.3% at Toronto-Bayview, 5.1% in Windsor, and 24.1% at the Princess Margaret Hospital.

**Hospital Statistics 1988-1989 published by the Ontario Ministry of Health.*

TABLE I

Annual Number of New Cases of Malignant Neoplasms in Males, by Site of Disease and Age at Diagnosis, Ontario 1988

SITE OF DISEASE	ICD9[1] NUMBER	AGE AT DIAGNOSIS (YEARS)																		Rank[2]
		0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75+	Unknown	All Ages	
Lip and oral cavity	140-145	1	0	0	1	4	6	9	17	24	25	45	72	97	74	66	122	1	564	10
Pharynx	146-148	0	0	0	1	1	0	7	3	16	9	34	39	33	26	18	19	0	206	
Esophagus	150	0	0	1	0	0	2	1	1	3	7	24	39	48	43	36	59	0	264	
Stomach	151	0	0	0	0	0	1	4	4	13	19	34	61	87	99	100	201	1	624	8
Intestine, except rectum	152, 153	0	0	0	1	2	5	9	25	30	59	112	188	277	370	340	600	6	2,024	3
Rectum and anus	154	0	0	0	0	2	3	2	11	7	35	73	103	147	153	159	205	1	901	5
Pancreas	157	0	0	0	0	0	0	0	4	15	18	21	45	73	92	78	154	0	500	
Nasal cavities,middle ear and accessory sinuses	160	0	1	0	0	0	0	0	1	2	2	4	3	7	3	7	11	0	41	
Larynx	161	0	0	0	0	0	0	2	0	5	16	31	47	64	62	38	47	3	315	
Trachea, bronchus and lung	162	1	1	0	0	3	3	7	20	51	112	223	415	659	756	615	918	3	3,787	1
Bone	170	0	4	6	12	4	7	3	1	4	3	1	3	6	3	2	7	0	66	
Connective tissue	171	4	1	4	5	3	10	5	7	7	5	6	15	10	9	11	26	1	129	
Malignant melanoma of skin	172	2	0	1	6	7	26	40	53	71	35	56	64	82	66	45	63	5	622	9
Prostate	185	5	0	0	0	1	0	0	0	1	12	41	156	393	623	665	1,424	5	3,326	2
Testis	186	1	0	0	9	21	61	40	26	25	10	3	6	4	2	3	3	0	214	
Bladder	188	1	2	1	0	0	9	10	10	35	41	73	142	196	249	237	423	4	1,433	4
Kidney and other urinary	189	4	2	0	1	3	4	4	15	33	39	59	77	96	78	84	126	0	625	7
Brain and other nervous system	191,92	17	17	6	10	11	16	20	22	33	20	26	35	47	57	26	55	1	419	
Thyroid gland	193	0	2	1	4	2	7	9	13	5	8	10	3	10	12	5	6	0	97	
Lymphosarcoma and reticulosarcoma	200	3	5	3	10	9	4	16	17	31	24	26	38	61	55	56	74	0	432	
Hodgkin's disease	201	0	1	6	16	28	25	17	11	4	11	5	11	13	8	12	7	0	175	
Other lymphomas	202	2	1	3	4	3	9	14	18	25	22	24	24	21	44	47	44	0	305	
Multiple myeloma	203	0	0	0	0	0	0	0	1	7	8	11	27	39	45	41	85	0	264	
Leukemia	204-208	23	12	11	10	9	14	8	18	17	23	28	35	55	88	103	177	4	635	6
Other and non-specific	Residual	17	7	3	4	9	8	18	20	34	55	93	146	208	225	213	405	10	1,475	
TOTAL	140-208[3]	81	56	46	94	122	220	245	318	498	618	1,063	1,794	2,733	3,242	3,007	5,261	45	19,443	

[1] ICD9: International Classification of Diseases, Ninth Revision, World Health Organization, Geneva, 1977.

[2] Rank order for 10 most common sites (or site groups).

[3] Excluding non-melanotic skin cancers (ICD9 number 173).

TABLE II

Annual Number of New Cases of Malignant Neoplasms in Females, by Site of Disease and Age at Diagnosis, Ontario 1988

SITE OF DISEASE	ICD9[1] NUMBER	AGE AT DIAGNOSIS (YEARS)																		Rank[2]
		0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75+	Unknown	All Ages	
Lip and oral cavity	140-145	2	1	0	0	2	2	5	5	9	13	13	15	20	33	34	73	0	227	
Pharynx	146-148	0	0	0	0	1	2	1	6	3	4	10	13	20	11	4	13	0	88	
Esophagus	150	0	0	0	0	0	0	2	1	0	1	2	10	4	23	20	53	0	116	
Stomach	151	0	1	1	0	1	1	0	8	9	8	14	17	33	53	55	147	0	347	
Intestine, except rectum	152, 153	0	0	0	1	3	2	8	15	35	74	105	142	230	279	299	806	1	2,000	2
Rectum and anus	154	0	0	0	1	1	2	4	7	15	26	48	61	80	109	105	233	3	695	6
Pancreas	157	0	0	0	0	0	3	3	3	3	11	13	33	46	88	71	205	0	479	
Nasal cavities, middle ear and accessory sinuses	160	0	0	0	0	0	2	1	0	1	0	4	5	5	2	5	5	0	30	
Larynx	161	0	0	0	1	2	0	1	3	1	7	4	15	13	8	14	11	0	80	
Trachea, bronchus and lung	162	0	0	0	1	2	3	8	19	44	97	136	211	327	373	311	432	1	1,965	3
Bone	170	2	1	4	9	1	4	3	3	4	2	5	3	5	2	6	7	1	62	
Connective tissue	171	2	3	1	3	4	7	6	3	5	7	8	10	8	14	10	21	0	112	
Malignant melanoma of skin	172	0	1	1	3	13	47	42	47	66	52	37	46	36	47	34	63	2	537	9
Breast	174	1	0	0	0	3	28	97	226	377	484	481	552	643	653	530	1,013	12	5,100	1
Cervix uteri	180	0	0	0	1	7	34	73	90	64	49	39	29	36	49	37	58	3	569[3]	7
Body of uterus	182	0	0	0	0	1	7	10	24	26	41	88	137	166	193	152	196	0	1,041	4
Other and unspecified uterus	179, 181	0	0	0	0	0	3	3	0	0	4	2	2	4	5	3	13	1	40	
Ovary and fallopian tube	183	1	0	4	7	11	24	23	46	44	54	72	100	101	92	76	175	2	832	5
Bladder	188	0	0	0	0	1	2	5	6	9	15	27	37	67	74	83	179	0	505	10
Kidney and other urinary	189	11	3	0	0	0	5	5	10	18	12	30	35	60	56	47	98	2	392	
Brain and other nervous system	191, 192	19	6	4	6	7	8	13	18	18	25	16	29	39	40	34	59	0	341	
Thyroid gland	193	0	0	3	13	24	30	35	34	23	34	13	20	12	18	16	23	0	298	
Lymphosarcoma and reticulosarcoma	200	1	2	2	2	2	7	3	5	18	13	28	37	30	56	43	100	1	350	
Hodgkin's disease	201	0	2	5	20	30	29	10	6	5	6	2	3	2	4	8	5	1	138	
Other lymphomas	202	2	0	0	3	5	3	6	11	14	21	18	31	33	39	34	78	1	299	
Multiple myeloma	203	0	1	0	0	0	0	1	2	5	8	12	18	29	33	50	68	0	227	
Leukemia	204-208	27	15	4	10	10	11	11	8	16	28	14	32	50	47	75	199	1	558	8
Other and non-specific	Residual	13	0	2	8	7	14	18	37	30	43	65	100	144	194	191	517	9	1,392	
TOTAL	140-208[4]	81	35	31	89	138	280	397	643	862	1,139	1,306	1,743	2,243	2,595	2,347	4,850	41	18,820	

[1] ICD9: International Classification of Diseases, Ninth Revision, World Health Organization, Geneva, 1977.
[2] Rank order for 10 most common sites (or site groups).
[3] Approximately 10% non-invasive cancer of the cervix.
[4] Excluding non-melanotic skin cancers (ICD9 number 173).

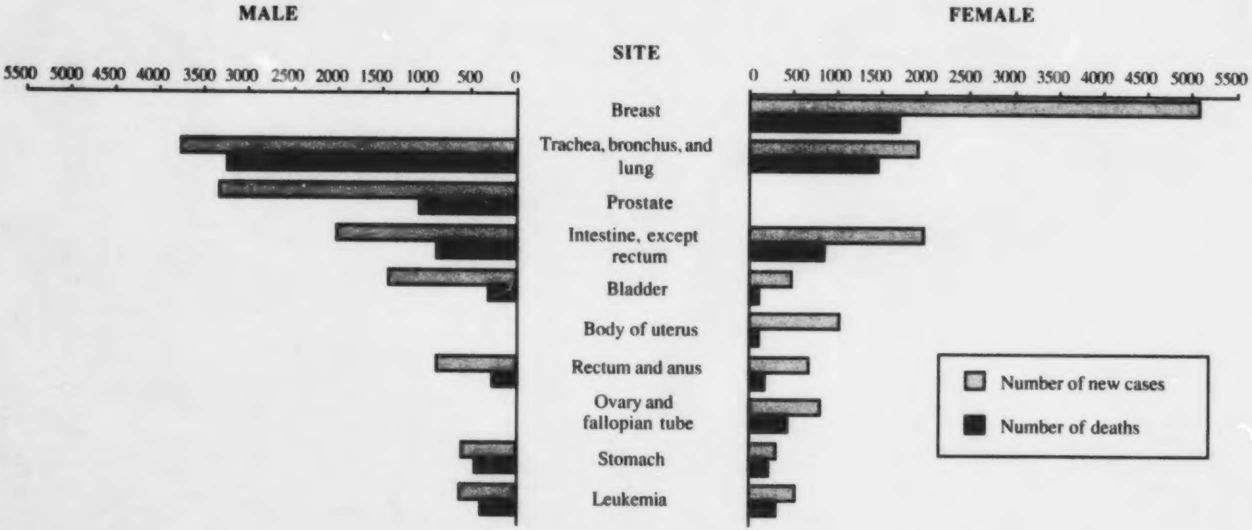


Fig. 1. New cases of, and deaths due to, malignant neoplasms, by sex and site of disease, for common cancers, Ontario 1988

TABLE III

Age-adjusted Rates[1] and Cumulative Risks (age 0-74)[2], Incidence (I) and Mortality (M) from Malignant Neoplasms in Males, by Site and Age, Ontario 1988

SITE OF DISEASE	ICD9[3] NUMBER	INCIDENCE/ MORTALITY	AGE AT DIAGNOSIS/DEATH (YEARS)							CR[2] 0-74
			0-14	15-29	30-44	45-59	60-74	75+	All Ages	
Lip and oral cavity	140-145	I	0.1	0.9	4.7	18.7	47.7	80.0	9.8	1.12
		M	0.0	0.2	0.4	4.2	13.8	22.4	2.4	0.29
Pharynx	146-148	I	0.0	0.2	2.5	10.8	15.6	13.0	3.8	0.45
		M	0.1	0.2	0.1	3.4	9.4	5.7	1.6	0.21
Esophagus	150	I	0.1	0.2	0.5	9.1	25.5	37.4	4.6	0.56
		M	0.0	0.0	0.7	10.7	29.4	43.8	5.3	0.65
Stomach	151	I	0.0	0.1	2.0	14.9	56.9	134.5	10.4	1.20
		M	0.0	0.0	1.4	8.3	38.9	133.7	7.7	0.80
Intestine, except rectum	152, 153	I	0.0	0.6	6.0	47.0	196.0	400.0	33.9	4.06
		M	0.0	0.0	1.2	17.1	83.8	228.0	14.9	1.66
Rectum and anus	154	I	0.0	0.4	1.9	27.9	91.5	131.6	15.5	1.96
		M	0.0	0.1	0.4	4.4	27.3	70.4	4.6	0.53
Pancreas	157	I	0.0	0.0	1.9	11.0	48.4	102.0	8.4	0.98
		M	0.0	0.0	1.8	9.3	44.8	99.6	7.8	0.91
Larynx	161	I	0.0	0.0	0.7	12.4	33.1	31.1	5.6	0.71
		M	0.0	0.0	0.0	4.0	16.2	26.6	2.6	0.31
Trachea, bronchus and lung	162	I	0.2	0.5	7.5	97.6	405.5	595.8	64.6	8.14
		M	0.0	0.2	5.2	74.2	348.2	585.6	55.2	6.60
Bone	170	I	0.9	2.1	0.7	1.0	23	4.5	1.4	0.10
		M	0.4	0.4	0.3	0.7	0.6	0.0	0.4	0.03
Malignant melanoma of skin	172	I	0.3	3.1	15.3	20.8	39.0	40.1	11.1	1.19
		M	0.0	0.3	1.9	4.7	7.6	11.4	2.0	0.23
Prostate	185	I	0.6	0.1	0.1	26.0	331.6	957.6	53.1	6.05
		M	0.0	0.0	0.0	4.3	81.3	448.8	16.9	1.52
Testis	186	I	0.1	7.1	8.2	2.6	1.8	2.5	3.9	0.30
		M	0.0	0.9	0.4	0.3	0.8	2.1	0.4	0.04
Bladder	188	I	0.4	0.7	5.2	33.3	135.5	281.0	24.1	2.85
		M	0.0	0.0	0.5	2.4	23.4	117.8	4.9	0.45
Kidney and other urinary	189	I	0.7	0.6	5.0	23.4	51.7	80.9	11.0	1.28
		M	0.1	0.1	1.1	6.3	20.5	51.9	4.1	0.44
Brain and other nervous system	191, 192	I	4.2	3.1	7.0	10.9	26.2	33.9	8.0	0.77
		M	1.6	0.8	3.5	9.9	23.4	26.5	5.5	0.59
Thyroid gland	193	I	0.3	1.1	2.4	3.0	5.4	4.2	1.8	0.18
		M	0.0	0.0	0.0	0.3	1.0	1.9	0.2	0.02
Lymphosarcoma and reticulosarcoma	200	I	1.1	2.0	6.0	11.8	34.4	48.1	7.8	0.87
		M	0.2	0.2	0.3	1.6	3.5	7.5	0.9	0.10
Hodgkin's disease	201	I	0.6	5.8	2.8	3.7	6.6	4.5	3.4	0.30
		M	0.0	1.0	0.6	1.1	3.2	1.2	0.8	0.10
Other lymphomas	202	I	0.6	1.3	5.3	9.6	22.0	29.3	5.5	0.63
		M	0.2	0.6	2.9	7.4	22.0	43.7	4.7	0.53
Multiple myeloma	203	I	0.0	0.0	0.8	6.0	24.9	57.9	4.4	0.51
		M	0.0	0.0	0.2	1.8	16.3	33.4	2.4	0.29
Leukemia	204-208	I	4.8	2.8	4.0	11.6	48.4	119.7	11.4	1.18
		M	1.1	1.0	1.5	8.2	28.5	107.0	6.8	0.67
ALL SITES[4]	140-208[4]	I	19.0	35.8	99.2	456.4	1,788.2	3,490.6	331.9	38.55
		M	4.8	6.9	28.0	209.3	957.1	2,347.4	172.7	17.78

[1] Age-adjusted by the direct method to the World Standard Population (See Table VII), expressed per 100,000 persons.

[2] Cumulative risk (CR) approximates the percent probability of a cancer diagnosis/death occurring by age 74 (Reference: Day NE. International Agency for Research on Cancer (IARC) Scientific Publication No. 15. pp. 443-52, 1976).

[3] ICD9: International Classification of Diseases, Ninth Revision, World Health Organization, Geneva, 1977.

[4] Excluding non-melanotic skin cancers (ICD9 number 173). Note that any individual sites not specifically included in the table are included in "ALL SITES".

TABLE IV

Age-adjusted Rates[1] and Cumulative Risks (age 0-74)[2], Incidence (I) and Mortality (M) from Malignant Neoplasms in Females, by Site and Age, Ontario 1988

SITE OF DISEASE	ICD9[3] NUMBER	INCIDENCE/ MORTALITY	AGE AT DIAGNOSIS/DEATH (YEARS)							CR[2] 0-74
			0-14	15-29	30-44	45-59	•60-74	75+	All Ages	
Lip and oral cavity	140-145	I	0.3	0.3	1.7	5.6	14.2	27.5	3.2	0.36
		M	0.0	0.1	0.5	1.2	5.2	6.9	0.9	0.11
Pharynx	146-148	I	0.0	0.2	0.9	3.6	6.3	4.9	1.4	0.16
		M	0.0	0.0	0.1	0.4	2.3	3.0	0.4	0.05
Esophagus	150	I	0.0	0.0	0.2	1.6	7.5	19.5	1.4	0.16
		M	0.0	0.0	0.5	1.2	8.2	20.4	1.4	0.16
Stomach	151	I	0.1	0.2	1.6	5.2	23.1	53.8	4.3	0.49
		M	0.0	0.0	0.9	4.4	14.6	45.9	3.0	0.33
Intestine, except rectum	152, 153	I	0.0	0.5	5.5	42.7	133.9	299.0	25.6	2.93
		M	0.0	0.1	1.4	16.1	53.0	156.4	10.6	1.14
Rectum and anus	154	I	0.0	0.3	2.4	17.9	48.7	85.9	9.3	1.11
		M	0.0	0.1	0.4	3.0	13.9	34.6	2.5	0.27
Pancreas	157	I	0.0	0.2	0.8	7.4	33.7	76.8	5.9	0.69
		M	0.0	0.0	0.3	5.8	30.3	77.0	5.2	0.58
Larynx	161	I	0.0	0.3	0.4	3.4	5.9	4.1	1.3	0.16
		M	0.0	0.0	0.0	0.6	1.7	2.8	0.3	0.04
Trachea, bronchus and lung	162	I	0.0	0.5	6.7	58.7	169.9	165.9	28.7	3.69
		M	0.0	0.1	4.1	41.2	120.1	152.3	20.8	2.64
Bone	170	I	0.7	1.4	0.9	1.4	2.2	2.7	1.2	0.10
		M	0.2	0.4	0.1	0.1	0.8	0.7	0.3	0.02
Malignant melanoma of skin	172	I	0.2	4.9	14.1	18.5	19.6	23.5	8.8	0.87
		M	0.0	0.3	1.1	2.3	4.0	4.7	1.1	0.12
Breast	174	I	0.1	2.3	65.4	206.4	309.1	378.1	78.7	8.91
		M	0.0	0.4	13.8	58.5	106.5	180.7	24.6	2.74
Cervix uteri	180	I	0.0	3.2	20.2	16.4	20.4	22.1	9.2	0.91
		M	0.0	0.4	3.5	4.9	11.9	15.3	2.8	0.34
Other uterus	179, 181, 182	I	0.0	0.8	5.8	35.8	88.1	78.6	16.1	2.05
		M	0.0	0.0	0.2	1.9	12.0	30.6	2.0	0.23
Ovary and other uterine adnexa	183	I	0.5	3.4	10.3	30.1	45.8	65.5	12.8	1.38
		M	0.0	0.2	2.5	12.5	35.6	45.4	6.5	0.79
Bladder	188	I	0.0	0.2	1.8	10.4	37.2	66.6	6.6	0.80
		M	0.0	0.0	0.2	0.9	7.6	34.3	1.5	0.14
Kidney and other urinary	189	I	1.6	0.4	3.1	10.2	27.7	35.6	5.9	0.66
		M	0.1	0.1	0.3	2.8	8.2	25.8	1.8	0.18
Brain and other nervous system	191, 192	I	3.3	1.8	4.4	9.4	19.1	22.0	5.8	0.58
		M	1.3	0.8	1.8	5.1	14.3	17.0	3.3	0.35
Thyroid gland	193	I	0.3	5.6	8.1	9.3	7.6	8.3	5.2	0.47
		M	0.0	0.0	0.0	0.4	1.3	4.6	0.3	0.03
Lymphosarcoma and reticulosarcoma	200	I	0.5	0.9	2.5	10.3	21.3	37.2	5.0	0.57
		M	0.1	0.2	0.2	0.6	2.2	6.5	0.6	0.05
Hodgkin's disease	201	I	0.7	6.8	1.8	1.5	2.2	1.8	2.7	0.20
		M	0.0	0.6	0.6	0.4	0.4	1.8	0.4	0.03
Other lymphomas	202	I	0.2	1.0	2.8	9.4	17.8	29.2	4.4	0.49
		M	0.1	0.6	1.8	4.0	13.5	34.7	3.0	0.33
Multiple myeloma	203	I	0.1	0.0	0.8	5.0	18.3	25.2	3.1	0.40
		M	0.0	0.0	0.0	2.0	12.3	22.0	1.8	0.23
Leukemia	204-208	I	5.2	2.7	3.2	10.0	28.3	73.3	8.4	0.78
		M	1.0	1.3	2.0	5.2	17.3	51.6	4.4	0.44
ALL SITES[4]	140-208[4]	I	16.3	41.7	174.8	562.0	1,202.8	1,897.7	275.6	31.20
		M	4.0	6.4	38.4	193.5	571.6	1,160.0	113.4	12.20

[1] Age-adjusted by the direct method to the World Standard Population (See Table VII), expressed per 100,000 persons.

[2] Cumulative risk (CR) approximates the percent probability of a cancer diagnosis/death occurring by age 74 (Reference: Day NE. International Agency for Research on Cancer (IARC) Scientific Publication No. 15, pp. 443-52, 1976).

[3] ICD9: International Classification of Diseases, Ninth Revision, World Health Organization, Geneva, 1977.

[4] Excluding non-melanotic skin cancers (ICD9 number 173). Note that any individual sites not specifically included in the table are included in "ALL SITES".

It should be noted that a "new case" registered at an OCTRF Regional Cancer Centre and the OCI/PMH refers to a case of cancer seen for the first time during that year at any one of the centres. If a case is seen at two centres in the same year, the case is recorded as seen only by the first centre (1.6% of cases were seen at more than one centre in the same year).

The location of the peripheral clinics associated with the OCTRF Regional Cancer Centres and the OCI/PMH, and the type of outreach program, determine the referral pattern to each (Table X). Thus, in Lambton County, of the 333 cases resident in the county, 331 were referred to the London Centre and only a small number to other centres. On the other hand, in Halton Regional Municipality, of the 620 cases resident in that area, 389 were referred to the Hamilton Centre, 173 to OCI/PMH and 45 were referred to the Toronto-Bayview Centre. From the Province of Quebec, 497 residents were referred to OCTRF Regional Cancer Centres; most were seen at the Ottawa Centre. An additional 185 residents of other provinces were seen in Ontario, principally at the OCI/PMH. Of the 167 residents of the USA and other countries treated in Ontario, most were seen at the OCI/PMH, and the Toronto-Bayview and Ottawa Centres.

The data in Tables VIII-X were extracted from the OCTRF Regional Cancer Centres in August 1990. Data extracted later may differ slightly from those presented here.

ACKNOWLEDGEMENTS

We acknowledge with gratitude the continuing co-operation of government. The Ontario Ministry of Health has provided source records and advice; the Office of the Registrar General of the Ministry of Consumer and Commercial Relations has provided computerized data on deaths due to all causes in Ontario residents and, in addition, has provided facilities for an on-site search of their records for treatment evaluation and other research. We appreciate the assistance of the staff of the Hospital Medical Records Institute (HMRI) and are indebted to the medical records staff of all hospitals in Ontario who willingly and promptly provide additional information, primarily for the generation of incidence data, but also to ensure the high quality of data entered in the Ontario Cancer Registry.

We extend special thanks to the Chief Executive Officers of the OCTRF Regional Cancer Centres and the OCI/PMH and their managers of health records for support during the year, and to the members of the Foundation's Standing Committee on Records and Statistics and its subcommittees.

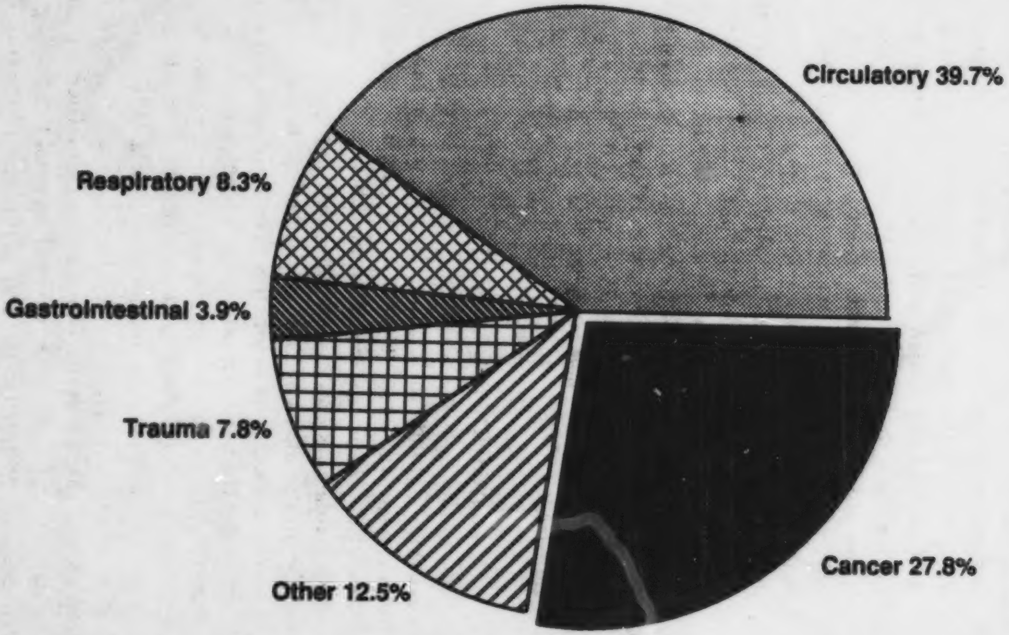


Fig. 2. Percentage distribution of major causes of death in males, Ontario 1989.

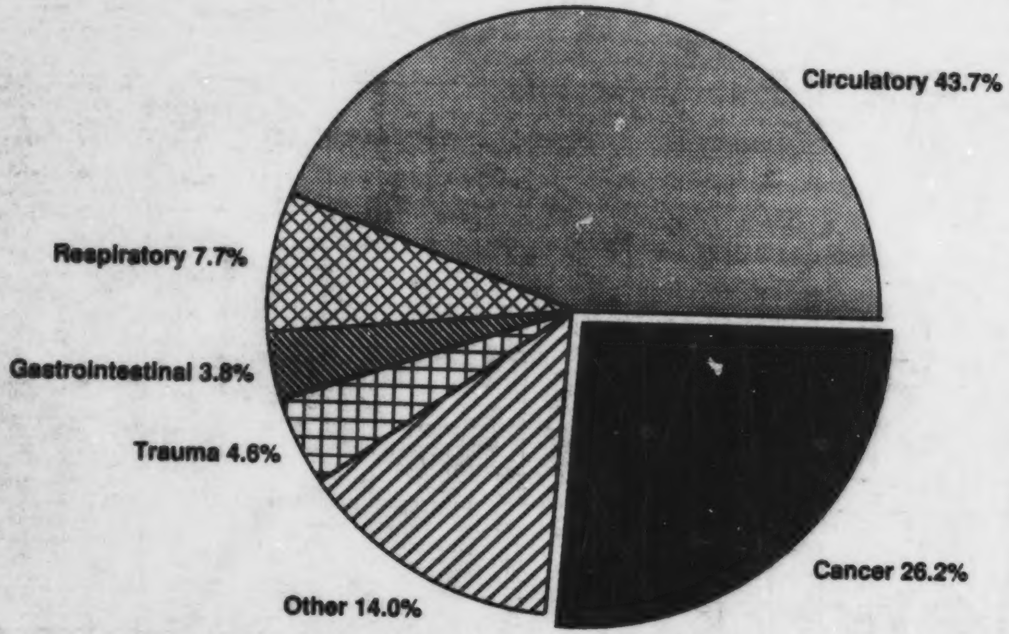


Fig. 3. Percentage distribution of major causes of death in females, Ontario 1989.

TABLE V

Number of Deaths due to Malignant Neoplasms in Males, by Site of Disease and Age at Death, Ontario 1989

SITE OF DISEASE	ICD9[1] NUMBER	AGE AT DEATH (YEARS)																	Rank[2]
		0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75+	All Ages	
Lip and oral cavity	140-145	0	0	0	0	0	0	0	1	5	2	7	22	28	12	16	37	130	
Pharynx	146-148	0	0	0	0	0	0	1	0	0	4	10	12	9	14	11	14	75	
Esophagus	150	0	0	0	0	0	0	0	1	4	4	10	29	58	42	31	75	254	
Stomach	151	0	0	0	0	0	1	2	3	10	18	24	28	56	86	71	176	475	4
Intestine, except rectum	152, 153	0	0	0	0	0	2	3	5	5	19	36	73	123	145	159	355	925	3
Rectum and anus	154	0	0	0	0	0	1	0	2	7	9	12	28	38	54	39	87	277	8
Pancreas	157	0	0	0	0	0	0	0	4	11	14	29	49	69	71	69	149	465	5
Nasal cavities, middle ear and accessory sinuses	160	0	0	0	0	0	0	0	1	0	0	2	2	0	3	1	4	13	
Larynx	161	0	0	0	0	0	0	0	1	2	3	12	12	21	29	20	37	137	
Trachea, bronchus and lung	162	0	0	1	1	0	3	5	14	39	75	171	329	512	626	536	960	3,272	1
Bone	170	0	0	1	5	1	0	1	2	0	0	1	1	3	0	1	2	18	
Connective tissue	171	0	0	0	0	0	1	3	4	1	1	2	3	7	5	4	16	47	
Malignant melanoma of skin	172	0	0	0	0	2	4	3	10	19	4	15	19	15	22	14	24	151	
Breast	175	0	0	0	0	0	0	0	0	0	0	1	1	1	0	0	6	9	
Prostate	185	0	0	0	0	1	0	0	0	2	0	2	28	71	142	215	625	1,086	2
Testis	186	0	0	0	1	1	1	4	4	1	1	2	0	1	0	0	2	18	
Bladder	188	0	0	0	0	0	0	0	0	1	6	5	13	40	40	51	177	333	7
Kidney and other urinary	189	0	1	0	0	0	2	0	0	6	14	10	28	26	33	29	72	221	
Brain and other nervous system	191, 192	3	2	2	5	4	5	5	11	22	12	16	43	39	34	33	40	276	9
Thyroid gland	193	0	0	0	0	0	0	0	0	2	2	1	2	2	3	3	4	19	
Lymphosarcoma and reticulosarcoma	200	0	0	0	0	0	1	1	0	2	3	1	4	5	3	3	11	34	
Hodgkin's disease	201	0	0	0	1	5	4	6	2	2	2	4	4	5	2	3	4	44	
Other lymphomas	202	1	2	0	3	3	3	1	8	9	11	18	22	38	35	44	66	264	10
Multiple myeloma	203	0	0	0	0	0	0	1	0	1	5	5	9	17	23	35	77	173	
Leukemia	204-208	6	2	4	9	6	4	3	10	17	5	11	16	40	41	41	128	343	6
Other and non-specific	Residual	5	2	1	1	0	2	10	11	12	34	56	91	169	199	174	423	1,190	
TOTAL	140-208[3]	15	9	9	26	23	34	49	94	180	248	463	868	1,393	1,664	1,603	3,571	10,249	

[1] ICD9: International Classification of Diseases, Ninth Revision, World Health Organization, Geneva, 1977.

[2] Rank order for sites with more than 100 deaths.

[3] Omitted are 30 deaths due to non-melanotic cancer of the skin (ICD9 number 173).

TABLE VI

Number of Deaths due to Malignant Neoplasms in Females, by Site of Disease and Age at Death, Ontario 1989

SITE OF DISEASE	ICD9[1] NUMBER	AGE AT DEATH (YEARS)																	Rank[2]
		0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75+	All Ages	
Lip and oral cavity	140-145	0	0	0	1	0	0	1	0	1	1	3	5	6	8	14	31	71	
Pharynx	146-148	0	0	0	0	1	0	0	0	2	2	0	3	3	5	4	4	24	
Esophagus	150	0	0	0	0	0	0	0	2	0	0	6	14	10	22	16	54	124	
Stomach	151	0	0	1	0	0	1	1	3	8	8	11	14	25	38	30	153	293	7
Intestine, except rectum	152, 153	0	0	0	0	0	0	3	6	5	18	38	51	87	115	125	424	872	3
Rectum and anus	154	0	0	0	0	0	0	1	0	2	5	9	13	16	26	29	81	182	
Pancreas	157	0	0	0	0	0	0	2	3	5	7	10	28	47	66	80	222	470	5
Nasal cavities, middle ear and accessory sinuses	160	1	0	0	0	0	1	0	0	1	0	0	2	1	0	0	3	9	
Larynx	161	0	0	0	0	0	0	0	0	0	2	1	9	5	6	3	10	36	
Trachea, bronchus and lung	162	0	0	0	0	0	1	5	14	25	58	90	150	214	254	228	411	1,450	2
Bone	170	0	0	0	0	1	1	1	0	1	0	0	1	0	0	0	4	9	
Connective tissue	171	1	1	0	1	1	0	4	2	1	4	4	2	3	6	3	11	44	
Malignant melanoma of skin	172	0	0	0	0	1	3	5	5	7	8	1	8	6	9	6	24	83	
Breast	174	0	0	0	0	0	4	19	57	84	116	143	208	209	231	203	537	1,811	1
Cervix uteri	180	0	0	0	0	0	2	12	13	12	11	17	13	12	23	16	40	171	
Other uterus	179, 181, 182	0	0	0	0	0	0	1	0	0	3	10	10	22	29	41	82	198	9
Ovary and fallopian tube	183	0	0	0	0	0	0	4	9	10	22	42	39	57	79	69	156	487	4
Bladder	188	0	0	0	0	0	0	0	0	1	3	1	4	10	20	14	84	137	
Kidney and other urinary	189	3	0	0	0	0	1	3	1	3	4	8	9	17	18	25	62	154	
Brain and other nervous system	191, 192	4	3	0	1	2	1	4	5	10	10	15	18	33	27	27	37	197	10
Thyroid gland	193	0	0	0	0	0	0	1	0	0	0	2	2	1	3	2	17	28	
Lymphosarcoma and reticulosarcoma	200	0	0	0	0	1	0	0	1	1	1	1	2	1	7	5	13	33	
Hodgkin's disease	201	0	0	0	2	0	1	1	3	2	1	2	2	2	1	2	7	26	
Other lymphomas	202	0	0	0	0	1	3	4	6	7	12	7	17	24	42	43	101	267	8
Multiple myeloma	203	0	0	0	0	0	0	0	1	1	5	9	11	16	15	22	71	151	
Leukemia	204-208	3	5	2	5	3	3	5	12	12	12	6	14	16	35	38	140	311	6
Other and non-specific	Residual	1	1	0	1	2	2	3	9	12	32	41	66	87	182	141	502	1,082	
TOTAL	140-208[3]	13	10	3	11	13	24	80	152	213	345	477	715	930	1,267	1,186	3,281	8,720	

[1] ICD9: International Classification of Diseases, Ninth Revision, World Health Organization, Geneva, 1977.

[2] Rank order for sites with more than 100 deaths.

[3] Omitted are 19 deaths due to non-melanotic cancer of the skin (ICD9 number 173).

TABLE VII

World Standard Population and Estimated Population of Ontario, 1988 and 1989 (In Thousands)

AGE GROUP	WORLD STANDARD[1] MALE OR FEMALE	ONTARIO, 1988[2]		ONTARIO, 1989[2]	
		MALE	FEMALE	MALE	FEMALE
0-4	12.0	338.7	322.9	346.2	329.0
5-9	10.0	323.1	308.1	329.4	314.2
10-14	9.0	320.7	305.6	323.0	307.7
15-19	9.0	353.9	334.5	350.6	331.9
20-24	8.0	393.6	383.4	382.6	370.9
25-29	8.0	432.3	434.7	441.2	442.1
30-34	6.0	401.2	413.5	413.9	423.8
35-39	6.0	366.0	377.5	374.5	387.5
40-44	6.0	332.5	334.2	347.4	350.7
45-49	6.0	263.5	263.7	274.2	274.4
50-54	5.0	231.5	232.0	235.2	236.5
55-59	4.0	228.3	230.6	228.0	230.2
60-64	4.0	207.4	228.7	209.0	227.0
65-69	3.0	168.7	202.7	177.0	212.7
70-74	2.0	118.9	153.4	118.6	154.3
75-79	1.0	82.3	119.5	85.8	123.6
80-84	0.5	43.9	79.9	45.6	82.8
85+	0.5	26.7	67.9	27.5	69.8
TOTAL	100.0	4,633.3	4,792.8	4,709.6	4,869.1

[1] Muir C. et al (eds). Cancer Incidence in Five Continents, Vol V. World Health Organization, Geneva, 1987, p.792.

[2] Source: Statistics Canada.

We acknowledge with gratitude the assistance of all the staff of Information Systems in the processing of the Foundation's large data base. In particular, we thank the individuals working under the direction of Mr. Tom Broz.

Our special thanks are extended to Mrs. Mary Nemes, Manager of Provincial Programs Unit in the Division, Miss Darlene Dale, Manager of Operations, Cancer Registration Unit, and the staff of the Division for their dedication to the generation of incidence data and their continual effort to improve the quality of the Ontario Cancer Registry. We are also grateful to Dr. Van C. Nguyen who, with the help of Miss Janice Fleury, Miss Gayle Morrison and Ms. Cathy Koltun, prepared this report.

TABLE VIII
New Cancer Cases Registered by Treatment Centre, 1980-1989[1,2]

CENTRE	YEAR OF REGISTRATION									
	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989[3]
Hamilton	2,507	2,537	2,688	2,780	2,782	3,498	3,472	3,729	3,849	3,880
Kingston	984	997	1,073	1,226	1,195	1,238	1,316	1,434	1,370	1,630
London	2,583	2,529	2,563	2,748	2,950	3,080	3,011	3,315	3,286	3,478
Ottawa	2,078	2,190	2,248	2,573	2,847	2,929	2,963	3,117	3,327	3,446
Sudbury	–	–	–	–	–	–	285	311	508	488
Thunder Bay	401	462	444	435	506	505	513	552	565	648
Toronto-Bayview	441	504	816	1,251	1,826	2,264	2,774	2,982	3,460	3,553
Toronto, PMH	7,057	7,320	7,012	7,332	7,171	7,328	6,840	6,646	6,649	5,609
Windsor	813	907	858	960	1,038	1,053	1,095	1,137	1,208	1,289
TOTAL	16,864	17,446	17,702	19,305	20,315	21,895	22,269	23,223	24,222	24,021

[1] Excludes carcinoma of cervix in situ.

[2] Any case registered at more than one treatment centre in a given year is allocated to the centre where it was first registered.

[3] Data for the year 1989 were extracted from the centres in August 1990.

TABLE IX
New Cancer Cases Registered by Site of Disease and Treatment Centre, 1989[1]

SITE OF DISEASE	ICD9[2] NUMBER	TREATMENT CENTRE									TOTAL	
		Hamilton	Kingston	London	Ottawa	Sudbury	Thunder Bay	Toronto		Windsor	Number	Per Cent
								Bayview	PMH			
Lip	140	14	18	18	13	1	1	5	25	5	100	0.4
Tongue	141	25	7	29	34	1	4	21	60	7	188	0.8
Rest of mouth	142-145	52	14	44	37	3	7	41	103	14	315	1.4
Pharynx and tonsil	146-149	40	12	31	38	1	12	47	119	10	310	1.4
Esophagus	150	49	13	35	29	5	9	26	69	7	242	1.1
Stomach	151	52	6	24	52	6	10	27	51	15	243	1.1
Intestine, except rectum	152-153	132	43	154	197	30	44	89	207	73	969	4.3
Rectum and anal canal	154	127	50	135	128	14	32	87	250	44	867	3.9
Other digestive system	155-159	61	10	46	52	14	5	36	72	26	322	1.4
Nose, middle ear and accessory sinuses	160	7	–	6	6	–	2	5	29	–	55	0.2
Larynx	161	63	23	58	74	–	15	48	121	18	420	1.9
Lung, bronchus and trachea	162	490	226	502	527	131	112	567	729	164	3,448	15.4
Other respiratory	163-165	23	7	13	16	4	–	8	22	2	95	0.4
Bone	170	12	1	10	9	–	2	1	15	6	56	0.3
Malignant melanoma	172	133	30	70	70	16	12	179	120	25	655	2.9
Other cancer of skin	173	267	224	207	218	10	33	366	326	171	1,822	8.2
Breast	174-175	684	219	586	628	94	114	677	1,068	214	4,284	19.2
Cervix uteri	180	68	24	64	54	7	10	104	129	15	475	2.1
Other uterus	179-181-182	111	31	87	100	2	13	113	166	28	651	2.9
Ovary, tubes and ligament	183	98	27	63	98	15	13	124	100	26	564	2.5
Other female genital organs	184	24	4	13	19	–	1	28	18	4	111	0.5
Prostate	185	239	92	234	182	16	42	206	294	61	1,366	6.1
Testis	186	39	12	31	31	5	2	42	68	7	237	1.1
Other male genital organs	187	1	2	3	5	–	1	1	9	–	22	0.1
Bladder	188	70	22	42	49	4	8	59	106	24	384	1.7
Kidney and other urinary	189	35	13	61	41	5	16	45	59	14	289	1.3
Brain and nervous system	191-192	63	20	105	73	2	13	87	119	17	499	2.2
Thyroid gland	193	10	3	9	13	1	5	16	43	2	102	0.5
Lymphosarcoma and reticulum cell sarcoma	200	60	28	87	109	19	20	70	151	27	571	2.6
Hodgkin's disease	201	37	12	37	48	10	14	54	92	10	314	1.4
Other lymphomas	202	126	29	47	49	5	11	48	102	16	433	1.9
Leukemia	204-208	104	43	83	47	14	18	38	168	32	547	2.5
Other sites	Residual	320	52	181	163	39	41	148	360	59	1,363	6.1
TOTAL MALIGNANT		3,636	1,317	3,115	3,209	474	642	3,413	5,370	1,143	22,319	100.0
Cervix uteri (in-situ)	233.1	3	–	4	8	–	–	11	14	4	44	
Other sites (in-situ)	230-234	44	31	61	56	8	6	76	78	33	393	
Neoplasms of uncertain behavior	235-238	31	13	55	13	4	7 –	23	33	25	197	
Multiple skins (see text)	173	169	269	247	168	2	–	41	128	88	1,112	
Seen at more than one centre		–	33	63	50	17	–	81	83	25	352	

[1] Data extracted from the Centres in August 1990.

[2] ICD9 - International Classification of Diseases, Ninth Revision, World Health Organization, Geneva, 1977.

TABLE X

New Cancer Cases Registered by Place of Residence and Treatment Centre, 1989[1]

COUNTY, DISTRICT, OR REGIONAL MUNICIPALITY[2]	TREATMENT CENTRE									TOTAL
	Hamilton	Kingston	London	Ottawa	Sudbury	Thunder Bay	Toronto		Windsor	
							Bayview	PMH		
Algoma, DS	3	–	7	8	18	10	17	118	–	181
Brant	246	–	12	1	–	–	2	1	–	262
Bruce	5	–	151	–	–	–	1	13	1	171
Carleton, Ottawa RG	1	–	1	1,617	–	–	6	9	–	1,634
Cochrane, DS	7	6	–	32	13	15	16	89	–	178
Dufferin	4	–	–	1	–	–	18	36	1	60
Dundas	–	1	–	42	–	–	–	2	–	45
Durham, RG	4	33	6	1	–	1	156	300	1	502
Elgin	–	–	160	–	–	–	1	2	1	164
Essex	3	–	89	–	–	–	–	7	1,047	1,146
Frontenac	2	390	2	3	–	–	3	5	–	405
Glengarry	–	1	–	51	–	–	–	–	–	52
Grenville	1	28	–	43	–	–	1	1	–	74
Grey	5	–	179	1	–	–	13	43	–	241
Haldimand-Norfolk, RG	172	–	68	–	–	–	–	5	–	245
Haliburton	–	2	1	–	–	–	7	22	–	32
Halton, RG	389	–	7	3	–	2	45	173	1	620
Hastings	4	283	1	4	–	–	19	34	–	345
Huron	1	1	121	1	1	–	1	–	–	126
Kenora	2	1	2	–	1	49	–	2	–	57
Kent	–	1	213	–	–	–	–	2	27	243
Lambton	–	–	331	–	–	–	–	4	1	336
Lanark	–	36	–	124	–	–	–	2	–	162
Leeds	1	156	–	16	–	–	2	2	–	177
Lennox and Addington	–	86	–	2	–	–	–	1	–	89
Manitoulin, DS	–	–	–	–	11	1	–	6	–	18
Middlesex	4	4	926	–	–	–	1	11	1	947
Muskoka, RG	3	–	5	2	–	–	30	57	–	97
Niagara, RG	1,020	2	11	3	2	–	18	61	2	1,119
Nipissing, DS	–	3	2	8	18	7	16	134	–	188

TABLE X (continued)

New Cancer Cases Registered by Place of Residence and Treatment Centre, 1989[1]

COUNTY, DISTRICT, OR REGIONAL MUNICIPALITY[2]	TREATMENT CENTRE									TOTAL
	Hamilton	Kingston	London	Ottawa	Sudbury	Thunder Bay	Toronto		Windsor	
							Bayview	PMH		
Northumberland	2	43	4	1	–	–	39	85	–	174
Oxford	5	–	207	–	–	–	2	4	–	218
Parry Sound, DS	4	1	–	1	6	2	12	80	–	106
Peel, RG	20	5	2	12	–	1	252	525	7	824
Perth	1	–	162	–	–	–	–	3	–	166
Peterborough	3	42	1	6	–	–	46	170	–	268
Prescott	–	–	–	72	–	–	–	–	–	72
Prince Edward	–	84	–	1	1	–	4	8	–	98
Rainy River, DS	–	–	–	–	–	59	–	3	–	62
Renfrew	–	3	1	268	1	–	2	1	–	276
Russell	–	–	–	66	–	–	1	–	–	67
Simcoe	1	–	8	17	–	1	185	263	3	478
Stormont	1	4	–	155	1	–	–	1	–	162
Sudbury, RG and DS	5	5	9	38	367	12	21	171	2	630
Thunder Bay, DS	14	–	1	1	2	460	3	10	–	491
Timiskaming, DS	1	–	2	6	20	2	6	60	1	98
Victoria	–	19	–	1	1	–	30	96	–	147
Waterloo, RG	138	2	336	2	–	–	10	38	1	527
Wellington	232	1	39	–	–	–	6	17	–	295
Wentworth, Hamilton RG	1,103	1	3	–	–	1	2	12	2	1,124
York/Metro Toronto RG	20	11	9	69	3	16	2,322	2,543	25	5,018
Quebec	2	8	4	468	–	–	7	7	1	497
Other Provinces	14	23	17	28	5	1	24	72	1	185
U.S.A.	1	15	11	9	–	1	7	15	7	66
Other World	4	1	3	14	3	–	40	35	1	101
Residence at diagnosis not stated	188	15	1	11	–	1	19	9	9	253
TOTAL	3,636	1,317	3,115	3,209	474	642	3,413	5,370	1,143	22,319

---

[1] Data extracted from the Centres in August, 1990.

[2] DS = District, RG = Regional Municipality, others are Counties.

DIRECTORY

MEMBERS OF THE ONTARIO CANCER TREATMENT AND RESEARCH FOUNDATION AND ITS COMMITTEES

(As constituted at December 31, 1990)

THE OCTRF BOARD

Chairman:

Senator MICHAEL A. MEIGHEN, Q.C., LL.L.	Toronto

President and Chief Executive Officer:

J.W. MEAKIN, M.D.,C.M., M.A., FRCPC	Toronto

Members:

G.M. ADAMS	Thunder Bay
K.R. CLARKE, C.A.	Toronto
M.M. CONROY, B.Sc.N., Reg.N.	Toronto
G.P. ELIGH, B.Comm.	Kingston
S. GELLER, B.A.	Toronto
C.A.D.G. HURTEAU, M.D.,C.M., L.M.C.C., F.R.C.S.(C), F.A.C.O.G.	Ottawa
G. GENCHI	Mississauga
Rev. W.K. JAGGS, L.Th., M.A., D.Min.	Windsor
MRS. BETTE JOHNSTON, Reg.N.	Toronto
L.M. KUSHNIR, M.L.S., LL.B.	Toronto
W. LIVINGSTON, B.Comm.	Toronto
D.M. MacKENZIE, M.A., D.H.A.	Toronto
L. SIMINOVITCH, C.C., Ph.D., F.R.S.C., D.Sc.	Toronto
B.M. THALL, M.A.Sc., Ph.D.	Toronto
C. WAXMAN	Hamilton
D.B.WEBBER, B.B.A., F.C.S.I.	London
J.Y.K. WONG, M.D.	Toronto

Secretary:

H. WODINSKY, B.A., M.A., M.H.Sc.	Toronto

Treasurer:

N. Devereaux, C.G.A	Toronto

AUDIT AND FINANCE COMMITTEES

Chairman:

G.M. ADAMS	Thunder Bay

Vice-Chairman:

C. Waxman	Hamilton

Secretary:

H. Wodinsky, M.H.Sc.	Toronto

Members:

Senator M.A. Meighen, Q.C., LL.L.	Toronto
L. Kushnir, LL.B.	Toronto
W. Livingston, B.Comm.	Toronto
B.M. Thall, Ph.D.	Toronto

INVESTMENT COMMITTEE

Chairman:

D.B. Webber, B.B.A.	London

Secretary:

H. Wodinsky, M.H.Sc.	Toronto

Treasurer:

N. Devereaux, CGA	Toronto

Members:

W. Foote	Toronto
W.R. Livingston, B.Comm.	Toronto
J.W. Meakin, M.D.,C.M.	Toronto
J. Payzant, B.Comm.(Hon)	Toronto
B.M. Thall, Ph.D.	Toronto

CANCER RESEARCH ADVISORY PANEL

Chairman:

L. Siminovitch, C.C., Ph.D., D.Sc.	Toronto

Members:

R.G. Deeley, Ph.D	Kingston
E.A. Eisenhauer, M.D.	Kingston
G.L. Hammond, Ph.D.	London
P.G. Harding, M.D.	London
A.D. Ho, M.D.	Sudbury
R.S. Kerbel, Ph.D.	Toronto
M. Levine, M.D.	Hamilton
L.D. Marrett, Ph.D.	Toronto
R.S. Roberts, M.Tech.	Hamilton
B.C. Wilson, Ph.D.	Hamilton

CHEMOTHERAPEUTIC AGENTS COMMITTEE

Chairman:

TBA

Members:

H.T. Abu-Zahra, M.B.,B.Ch.	Windsor
B.J. Campling, M.D.	Kingston
H. Chan, M.B.,B.S.	Toronto
R.E.T. Corringham, M.B.,B.S.	Sudbury
C. Cripps, M.D.	Ottawa
R. Feld, M.D.	Toronto
M.T. Gannon, D.Sc.	Toronto
I.J. Kerr, M.D.	Toronto
W.I. Kocha, M.D.	London
P.B. McCulloch, M.D.	Hamilton
TBA	Thunder Bay

CONSULTANT PATHOLOGISTS COMMITTEE

Chairman:

TBA

Members:

R. Bonin, M.D.	Sudbury
N. Escott, M.D.	Thunder Bay
G.L. Frank, M.B.,Ch.B.	Hamilton
E.J. Holowaty, M.D.	Toronto
P.M. Manley, M.D.	Kingston
V.J. Montpetit, M.D.	Ottawa
H. Richmond, M.D.	Toronto
J.R. Srigley, M.D.	Toronto
V. Walley, M.D.	Ottawa
G.E. Yee, M.D.	Windsor

RECORDS AND STATISTICS COMMITTEE

Chairman:

E.A. Clarke, M.B.,B.S.	Toronto

Members:

T.D.R. Briant, M.D.	Toronto
W.R. Bruce, Ph.D., M.D.	Toronto
R. Feld, M.D.	Toronto
M. Goodyear, M.B.,B.S.	Hamilton
R.D.T. Jenkin, M.B.,B.S.	Toronto
W.I. Kocha, M.D.	London
J.F. Kotalik, M.D.	Thunder Bay
N. Kreiger, Ph.D.	Toronto
J.L. Pater, M.D.	Kingston
D. Ross, C.C.H.R.A.	London
TBA	Ottawa
S. Yoshida, M.D.	Windsor

SENIOR MANAGEMENT COMMITTEE

Chairman:

H. Wodinsky, M.H.Sc.	Toronto

Members:

E.A. Clarke, M.B.,B.S.	Toronto
R.E.T. Corringham, M.B.,B.S.	Sudbury
N.J. Devereaux, C.G.A.	Toronto
W.K. Evans, M.D.	Ottawa
M. Fuchs, M.H.Sc.	Toronto
A.D. Ginsburg, M.D.	Kingston
M.S. Hodgkinson	Toronto
W.M. Hryniuk, M.D.	Hamilton
R.D.T. Jenkin, M.M.B.,B.S.	Toronto
J.F. Kotalik, M.D.	Thunder Bay
J.C. Laidlaw, M.D.	Toronto
L. Levin, M.D.	London
L.V. MacLean, B.A.	Toronto
J.W. Meakin, M.D.,C.M.	Toronto
G.C.K. Mok, M.D.	Windsor
M. Muller, B.Arch	Toronto
C. Zylak, M.D.	Hamilton

FOUNDATION CORPORATE OFFICE STAFF

President and Chief Executive Officer:
J. William Meakin, M.D.,C.M.

Executive Vice-President and Chief Operating Officer:
Harold Wodinsky, M.H.Sc.

Vice-President OCTRF and Director Division of Epidemiology and Statistics:
E. Aileen Clarke, M.B.,B.S.

Vice-President Research and Education:
John C. Laidlaw, M.D.

Chief Financial Officer:
Nelson J. Devereaux, C.G.A.

Director, Strategic and Operational Planning:
Molly Fuch, M.H.Sc.

Director, Information Systems:
Martin Hodgkinson

Deputy Director/Manager of Operations Ontario Breast Screening Program:
Donna Lillie, B.A.

Director, Human Resources:
Loraine V. MacLean, B.A.

Director, Facilities Planning and Development:
W. Michael Muller, B.Arch.

Director, Ontario Breast Screening Program:
Carl Zylak, M.D.

Editor of Publications:
John O. Godden, M.D.,C.M.

APPENDICES

APPENDIX A

BEQUESTS AND OTHER DONATIONS

The Foundation was the grateful recipient of legacies, bequests and other donations totalling $1,738,486 for the fiscal year ending March 31, 1990, which are of inestimable value to the Foundation's program.

Legacies of $1,000 or over were received during the above period from the following estates:

The Late Archibald, Mabel Ethel, Toronto for Research	$ 5,873
-Atkinson, Norine, Bracebridge	24,462
-Bell, Elizabeth Ethel, Toronto construction of cancer centres	48,631
-Berry, Richard Morgan, London for cancer research at London Centre	1,392
-Brand, Gladys Irene, London for use at London Centre	1,520
-Brocklebank, J.A. Howson, Streetsville	150,000
-Brown, Thomas, London for use at London Centre	10,000
-Buck, Gerald Patrick, London for use at London Centre	1,500
-Clark, Robena Campbell, Acton	10,989
-Collamore, Arthur Grafton, Lamberth	3,720
-Cumming, Robert, Toronto	10,000
-Daley, Annie Gertrude, Toronto	5,000
-Dennis, Beecher, Toronto	18,218
-Durham, Elfred, Toronto for use in Research	7,584
-Dzida, Maria, North York	39,228
-Flatt, Ella Muriel, Toronto	26,439
-Freedman, John Jacob, Toronto	9,000
-Gardner, John Thomas, Hamilton for Research	1,000
-Garrett, Norman Parks, Clinton	4,577
-Gibson, Margaret Leona, Toronto	13,441

-Goering, Elma Louise, Hamilton for use at Hamilton centre for cancer research	5,500
-Gray, Florence Mabel, London for use at London	291,500
-Haivie, William Forrest, Windsor maintenance of equipment at Windsor Centre	250,000
-Haven, Edith Josephine, Kingsville	35,000
-Houston, Florence Campbell, Scarborough	1,165
-Johnson, Janet Eleanor, Brockville	2,500
-Kay, Laura Levenia, Beaverton for Research	48,577
-Kipkie, Boyd E.W., Kingston	130,122
-Kusiak, Julia, St.Catherines	1,000
-Langenfeld, Janina, Flamborough	44,000
-Langford, Clare Hobbs, London for use at London Clinic	5,000
-Mayers, Florence, Dresdon	1,479
-McEwen, Linda Mabel, London for use at London Centre	9,000
-Moore, Rosena Dorothy, Mississauga	15,675
-Myers, Florence Alexina, Windsor for Research	107,762
-Norton, Elizabeth Evelyn, Toronto	1,000
-O'Prey, Mary Jane, Toronto	17,500
-Popkie, Sarah Ann, Peterborough	4,057
-Richter, Bertha Mabel, London (Richter Endowment Fund) for use at London Clinic	154,000
-Sanderson, Clara B., Brantford	8,622
-Scott, Sadie L., Strathroy	1,000
-Sloan, William Norman, Islington	1,000
-Springer, Clarence Henry, Hamilton	1,000
-Victoria, Maude, Orangeville	1,000
-Whealey, Joseph Alfred, Toronto	359,726
-White, Wesley John, London for use in Cancer Research at London Centre	5,000

Donations of $1,000 or more were received from the following:

-Armstrong, Mrs. Ruth, Oakville for Research	1,000
-Digital Equipment of Canada, Kanata from baseball tournament	2,490
-Employees of The Oshawa Group Limited Etobicoke, 1989 contributions	2,956
-Employees of The Oshawa Group Limited Etobicoke, 1988 contributions	2,759
-Maylor, Mark, Etobicoke	1,000
-Murphy, June J., Willowdale from baseball tournament	10,635
-P.J. Ward Associates Ltd., Toronto	1,953
-Webster, John H., Toronto	2,620

The Foundation is grateful to these donors and to the many others not listed above and it reveres the memory of those who, when making their wills, extended beyond their lifetime the fight against cancer. These welcome additions to our research and other funds ensure that the Foundation's extensive cancer control programs can proceed at a time of financial constraints and inflated costs.

APPENDIX B

LIST OF ARTICLES PUBLISHED IN 1989 BY CAREER SCIENTISTS, RESEARCH ASSOCIATES, GRANTEES, MEMBERS OF THE OCTRF STAFFS AT THE REGIONAL CANCER CENTRES AND CORPORTATE OFFICE AND THE OCI/PMH

HAMILTON

OCTRF Hamilton Regional Cancer Centre:

Arnold AM, Johnstone B, Stoskopf B, Skingley P, Browman G: Recruiment for a n efficacy study in chemoprevention. *Prev Med* 1989; **18:** 700.

Browman GP, Arnold A, Booker L, Johnstone B, Skingley P, Levine MN: Etretinate blood levels to monitor compliance and contamination in a chemoprevention trial. *J Natl Cancer Inst* 1989; **81:** 795.

Clark DA, Hirte HW, Buick RN: Human ovarian carcinoma: Evidence for patient-related differences in susceptibility to cytotoxic effectors that attack different cellular subpopulations within a tumor. *Br J Cancer* 1988; **58:** 415.

Flock ST, Wilson BC, Patterson MS, Wyman DR: Monte Carlo modelling of light propagation in highly scattering tissues, I. Comparison with Diffusion Theory. *IEEE Trans Biomed Eng* 1989; **36:** 1164.

Flock ST, Wilson BC, Patterson MS, Wyman DR: Monte Carlo modelling of light propagation in highly scattering tissues, II. Comparison with measurements in phantoms. *IEEE Trans Biomed Eng* 1989; **36:** 1169.

Hirte HW, Intine RVA, Clark DA: Characterization of cells obtained from human ovarian carcinoma ascites after discontinuous percoll density gradient separation. *Proc Am Assoc Cancer Res* 1989; **30:** 110. (Abstract 434)

Hortobagyi GN, Hryniuk W, Frye D et al: Dose intensity analysis of high-dose (HD) chemotherapy for metastatic breast cancer (MBC). *Proc Am Assoc Cancer Res* 1989; **30:** 252.

Hryniuk WM: Correlation of dose intensity and prognosis in adjuvant chemotherapy: An extended controversy. *Recent Results Cancer Res* 1989; **115:** 17.

Jones GW: Wisdom and ethics: Making a choice. *Can Med Dent Soc Focus* 1989; **10:**8.

Kwok CS, Crivici A, MacGregor WD, Unger MW: Optimization of radioimmunotherapy using human malignant melanoma multicell spheroids as model. *Cancer Res* 1989; **49:** 3276.

Patterson MS, Chance B, Wilson BC: Time resolved reflectance for the non-invasive measurement of tissue optical properties. *Appl Optics* 1989; **28:** 2331.

Patterson MS, Schwartz E, Wilson BC: Quantitative Reflectance spectrophotometry for the noninvasive measurement of photosensitizer concentration in tissue during photodynamic therapy. *Proc SPIE* 1989; **1065:** 115.

Prestwich WV, Nunes J, Kwok CS: Beta dose point kernels for radionuclides of potential use in radioimmunotherapy. *J Nucl Med* 1989; **30:** 1036.

Wilson BC, van Lier JE: Radiolabelled photosensitizers for tumour imaging and photodynamic therapy. *J Photochem Photobiol* 1989; **B3:** 459.

Wilson BC: Photodynamic therapy: Light delivery and dosage for second generation photosensitizers. *In:* Photosensitizing Compounds: Their Chemistry, Biology and Clinical Use. New York: Wiley; 1989: 60.

Wilson BC, Park Y, Hefetz Y, Patterson MS, Madsen S, Jacques S: The potential of time-resolved reflectance measurements for the noninvasive determination of tissue optical properties. *Proc SPIE* 1989; **1064:** 97.

Wyman DR, Patterson MS, Wilson BC: Similarity relations for anisotropic scattering in Monte Carlo simmulations of deeply penetrating neutral particles. *J Comput Phys* 1989: **81:** 137.

Wyman DR, Patterson MS, Wilson BC: Similarity relations for the interaction parameters in radiation transport. *Appl Optics* 1989; **28:** 5243.

KINGSTON

OCTRF Kingston Regional Cancer Centre:

Bates DA, Mackillop WJ: The effect of hyperthermia on the uptake and cytotoxicity of melphalan in Chinese hamster ovary cells. *Int J Rad Oncol Biol Phys* 1989; **16:** 187.

Belch A, Shelley W, Bergsagel D et al: A randomized trial of maintenance versus no maintenance meophalan and prednison in responding multiple myeloma patients. *Br J Cancer* 1988; **57:** 94.

Blackstein ME, Eisenhauer E, Wierzbicki R: Epirubicin in extensive small cell lung cancer (ESCLC): A phase II study in patients without prior chemotherapy. University of Toronto, NCI(C) Clinical Trials Kingston and Nova Scotia Cancer Treatment Centre Halifax. *Proc Am Soc Clin Oncol* 1989; **8:** 385. (Abstract 859)

Brissette L, Young I, Narindrasorasak S, Kisilevsky R, Deeley RG: Differential induction of the SAA gene family in response to an inflammatory agent and to amyloid enhancing factor. *J Biol Chem* 1989; **264:** 19327.

Campling BG, Galbraith PR, Lam YM, Pym J: Use of the MTT assay for clinical chemosensitivity testing. *Proc Am Soc Clin Oncol* 1989. (Abstract 299)

Clark JW, Gurgo C, Franchini G, Gibbs WN, Lofters W et al: The molecular epidemiology of HTLV-I-associated non-Hodgkin's lymphomas in Jamaica. *Cancer* 1988; **61:** 1477.

Cochrane A, Deeley RG: Detection and characterization of degradative intermediates of avian apo very low density lipoprotein II mRNA present in estrogen treated birds and following destabilization by hormone-withdrawal. *J Biol Chem* 1989; **264:** 6495.

Cole SPC, Downes HF, Mirski SEL: Glutathione (GSH) levels are diminished but GSH-*S*-transferase and reductase activities are elevated in the multidrug resistant small cell lung cancer cell line, H69AR. *Proc Am Assoc Cancer Res* 1989; **30:** 2027.

Cole SPC, Downes HF, Slovak ML: Effect of calcium antagonists on the chemosensitivity of two multidrug resistant human tumour cell lines which do not overexpress P-glycoprotein. *Br J Cancer* 1989; **59:** 42.

Dinda M, Quirt CF, Mackillop WJ, Singer M: Freeze fracturing properties of native and heat adopted in Chinese hampster ovary (CHO) cells. *Biochem Cell Biol* 1989; **67:** 473.

Eisenhauer EA, Mackillop WJ: Focus on clinical trials. *In:* Stoll BA, ed. Cost/Benefit Controversies in Cancer Treatment. Basingstock Hampshire, England: The Macmillan Press Ltd.; 1988: Chapter 6.

Eisenhauer E, Quirt I, Cairncross G, Iscoe N, Swenerton K: Phase II evaluation of trimetrexate in four solid tumors. *Cancer Chemother Pharmacol* 1989; **23(Suppl):** C75.

Forkert PG, Vessey ML, Park SS, Gelboin HV, Cole SPC: Cytochromes P-450 in murine lung: an immunohistochemical study with monoclonal antibodies. *Drug Metab Dispos* 1989; **17:** 551.

Gerlach JH: Structure and function of P-glycoprotein. *In:* Ozols RF, ed. Drug Resistance in Cancer Therapy. Boston: Kluwer Academic Publishers; 1989: 37.

Ginsburg AD, Perrault DJ, Pritchard KI, Browman GP, McCulloch PB, Skillings J: Systemic adjuvant therapy for node-negative breast cancer. *Can Med Assoc J* 1989; **141:** 381.

Ginsburg LM, Quirt CF, Ginsburg AD, Mackillop WJ: Lung cancer patients: Perceptions of their illness and its treatment; *Br J Cancer* 1989; **61:** 184. (Abstract)

Kennedy JC, Pottier RH, Boyles J: Effect of pH on the partition of hematoporphyrin IX between isotonic citrate buffer or buffered human plasma, and either 1-octanol, human erythrocytes, or human lymphocytes. *Photochem Photobiol* 1989; **49:** 74S.

Leduc F, Brauch H, Hajj C, Dobrovic A, Kaye F, Gazdar A, Harbour JW, Pettengill OS, Sorenson GD, vanden Berg A, Kok K, Campling BG, Paquin F, Bradley WEC, Zbar B, Minna J, Buys C, Ayoub J: Loss of heterozygosity in a gene coding for a thyroid hormone receptor in lung cancer. *Am J Hum Genetics* 1989; **44:** 282.

Mackillop WJ, Dotsikas G: Cellular heterogeneity in human epithelial neoplasms. *Int J Cell Cloning* 1988; **6:** 161.

Mackillop WJ, Palmer MJ, O'Sullivan B, Ward GK, Steele R, Dotsikas G: Clinical trials in cancer: The role of surrogate patients in defining what constitutes an ethically acceptable clinical experiment. *Br J Cancer* 1989; **59:** 388.

Mackillop WJ, Palmer MJ, Ward GK, Dotsikas G, Osborne EJ, Quirt CF, O'Sullivan B: The expert surrogate system: A role for the golden rule in clinical practice. *Humane Med* 1988; **4:** 89.

Mackillop WJ, Quirt CF: Can oncologists predict the course of malignant disease in their individual patients? *Br J Cancer* 1989; **61:** 184. (Abstract)

Mackillop WJ, Quirt CF: Can oncologists predict the course of malignant disease in their individual patients? *Med Decis Making* 1989; **9:** 323. (Abstract)

Mackillop WJ, Stewart WE, Ginsburg AD, Stewart SS: Cancer patients' perceptions of their illness and its treatment. *Br J Cancer* 1988; **50:** 355.

Mirski SEL, Cole SPC: Antigens associated with multidrug resistance in H69AR, a small cell lung cancer cell line. *Cancer Res* 1989; **49:** 5719.

Mirski SEL, Cole SPC: Antigens associated with the development of resistance in H69AR, a multidrug resistant small cell lung cancer cell line. *Proc Am Assoc Cancer Res* 1989; **30:** 2043.

Murphy EL, Hanchard B, Figueroa JP, Gibbs WN, Lofters WS et al: Modelling the risk of adult T-cell leukemia/lymphoma in persons infected with human T-Lymphotropic Virus Type 1. *Int J Cancer* 1989; **43:** 250.

O'Dwyer PJ, Eisenhauer EA, King SA, Hoth DF, Grem JL: Hypersensitivity reactions to deoxycoformycin. *Cancer Chemother Pharmacol* 1989; **23:** 173.

Pottier RH, Kennedy JC: Photodiode array fluorescence technique for measuring drug clearance rates. *J Photochem Photobiol* 1989; **3:** 135.

Pottier RH, Kennedy JC, Weagle G, Paterson P, Biolo R, Jori G, Petryka ZJ: Clearance rates of porphyrin derivatives and Zn phthalocyanine. *Photochem Photobiol* 1989; **49:** 15S.

Rank GH, Goerzen DW, Gerlach JH: Crossed immunoelectrophoresis of major protein antigens during pupation of the leafcutting bee *Megachile rotundata. Apidologie* 1989; **20:** 139.

Shelley W, Carmichael J, Brown L, Fraser R, Kirk R, Krepart G, Levitt M, Roy M, Willan A, Wilson K: Adriamycin and cisplatin in the treatment of stage III and IV epithelial ovarian carcinoma. *Gynecol Oncol* 1988; **29:** 208.

Shelley W, Starreveld A, Carmichael J et al: The toxicity of abdominopelvic radiation in advanced ovarian carcinoma patients following cisplatin/cyclophosphamide therapy and second-look laparotomy. *Obstet Gynecol* 1988; **71:** 327.

LONDON

OCTRF London Regional Cancer Centre:

Barsky MF, Coates RK, Macdonald DR: Computed tomographic features of primary brain lymphoma. *J Can Assoc Radiat* 1989; **40:** 80.

Blackledge G, Van Oosterom A, Mouridsen HT, Bramwell V, Santoro A, Verweij J, Rouesse J, Souhami R, Wagener T, Buesa J, Steward WP, Spooner D, Van Unnik J, Thomas D, Sylvester R: The place of chemotherapy in the management of soft tissue sarcoma: Experiences of the EORTC Soft Tissue and Bone Sarcoma Group. *Clin Oncol* 1989; **1:**106.

Bramwell V, Quirt I, Warr D, Verma S, Young V, Knowling M, Eisenhauer E: Combination chemotherapy with doxorubicin, dacarbazine and ifosfamide in advanced adult soft tissue sarcoma. *J Natl Cancer Inst* 1989; **81:** 1496.

Bramwell V, Rouesse J, Steward W, Santoro A, Buesa J, Thomas D, Sylvester R: Reduced rate of local recurrence following CYVADIC in localised soft tissue sarcoma: An EORTC randomised trial. *Proc Am Soc Clin Oncol* 1989; **8:**320.

Cairncross JG: Lumbar puncture. *In:* Wittes RE, ed. Manual of Oncologic Therapeutics. Philadelphia: Lippincott; 1989: 31.

Cairncross JG: CNS staging. *In:* Wittes RE, ed. Manual of Oncologic Therapeutics. Philadelphia: Lippincott; 1989: 51.

Cairncross JG: Carcinomatous meningitis. *In:* Wittes RE, ed. Manual of Oncologic Therapeutics. Philadelphia: Lippincott; 1989: 419.

Cairncross JG: CNS emergencies. *In:* Wittes RE, ed. Manual of Oncologic Therapeutics. Philadelphia: Lippincott; 1989: 437.

Cairncross JG: Paraneoplastic syndromes. *In:* Wittes RE, ed. Manual of Oncologic Therapeutics. Philadelphia: Lippincott; 1989: 610.

Cairncross JG: Tumors of the nervous system. *In:* Kelley WN, ed. Textbook of Internal Medicine. Philadelphia: Lippincott; 1989: 2418.

Cairncross JG, Chambers AF: Glial filament expression does not predict malignant behaviour of rat astrocytoma cells. *Neurology* 1989; **39:** 310.

Cairncross JG, Chambers AF: Glial filament expression does not predict malignant behaviour of rat astrocytoma cells. *J Neuro-oncol* 1989; **7:** S9.

Cairncross JG, Macdonald DR: Treatment of oligodendrogliomas. *J Neurosurg* 1989; **70:** 155.

Chambers AF: DNA transfection, genetic instability, and metastasis. *In:* Liotta LA (volume editor). Influence of Tumor Development on the Host, Cancer Growth and Progression, Vol. III, (Kaiser HE, series editor). Dordrecht: Kluwer Academic Publishers; 1989: 97.

Connor AM, Waterhouse P, Khokha R, Denhardt DT: Characterization of a mouse mitogen regulated protein/proliferin gene: A member of the growth hormone/prolactin gene family. *Biochem Biophys Acta* 1989; **1009:** 75.

Gaspar LE, Cheung AYC, Allen HH: Cervical carcinoma: Treatment results and complications of extended field irradiation. *Radiology* 1989; **172:** 271.

Goettler DM, Levin L, Chey WY: Gut peptide hormone and prolactin release in high- and low-risk postmenopausal breast cancer patients. *Proc Am Soc Clin Oncol* 1989; **8:** 40. (Abstract 154)

Hammond GL: Molecular analyses of human corticosteroid binding globulin: Expression and gene structure. *Proc New York Acad Sci* 1988; **538:** 25.

Hammond GL: Molecular characteristics of plasma steroid binding proteins. *In:* Imura H, Shizume K, Yoshida S, eds. Progress in Endocrinology, vol. 2. Amsterdam: Excerpta Medica; 1988: 1305.

Hammond GL, Underhill DA, Rykse HM, Smith CL: The human sex hormone binding globulin gene contains exons for androgen binding protein and two other testicular messenger RNAs. *Mol Endocrinol* 1989; **3:** 1869.

Jennings MT, Jennings VDL, Asadourian LLH, Rosenblum M, Albino AP, Cairncross JG, Old LJ: Five novel cell surface antigens of CNS neoplasms. *J Neurol Sci* 1989; **89:** 63.

Johnston EA, Hammond AJ, Cairncross JG: Bilateral hypoglossal palsies—a late complication of curative radiotherapy. *Can J Neurol Sci* 1989; **16:** 198.

Khokha R, Denhardt DT: Matrix metalloproteinases and tissue inhibitors of metalloproteinases (TIMP): A review of their role in tumorigenesis and tissue invasion. *Invasion Metastasis* 1989; **9:** 391.

Khokha R, Waterhouse P, Yagel S, Lala PK, Overall CM, Norton G, Denhardt DT: Antisene RNA-induced reduction in murine TIMP levels confers oncogenicity on Swiss 3T3 cells. *Science* 1989; **243:** 947.

Koropatnick J, Leibbrandt MEI, Cherian MG: Organ-specific metallothionein induction by X-irradiation of mice. *Radiant Res* 1989; **119:** 356.

Levin L: Apparent drug resistance in ovarian cancer. *Proc Int Gynecol Cancer Soc* 1989; **2:** 170.

Macdonald DR: Paraneoplastic neurological syndromes. *Oncology* 1989; **3:** 66.

Macdonald DR, Cairncross JG: Chemotherapy as initial treatment for aggressive oligodendroglioma. *Neurology* 1989; **39:** 261.

Macdonald DR, O'Brien RA, Gilbert JJ, Cairncross JG: Metastatic anaplastic oligodendroglioma. *Neurology* 1989; **39:** 1593.

Mah E, Antolak J, Scrimger JW, Battista JJ: Experimental evaluation of a 2D and 3D electron pencil beam algorithm. *Phys Med Biol* 1989; **34:** 1179.

Mertens W, Bramwell V, Lala PK: Continuous oral indomethacin (Indo) and continuous venous infusion of interleukin-2 (IL-2) in renal carcinoma and melanoma patients: Unusual toxicity-radiation recall. *Proc Am Soc Clin Oncol* 1989; **8:** 188.

Pilepich MV, Krall JM, John MJ, Rubin P, Porter AT, Marcial VA, Martz LL: Hormonal cytoreduction in locally advanced carcinoma of the prostate treated with definitive radiotherapy: Preliminary results of RTOG 83-70. *Int J Radiant Oncol Biol Phys* 1989; **16:** 813.

Porter AT: Is radiotherapy of use in Stage C prostate cancer? *Prog Clin Biol Res* 1989: **305:** 211.

Sandison GA, Huda W, Savoie D, Battista JJ: Comparison of methods to determine electron pencil beam spread in tissue-equivalent media. *Med Phys* 1989; **16:** 881.

Seralini G-E, Underhill CM, Smith CL, Nguyen VTT, Hammond GL: Biological half-life and transfer of maternal corticosteroid binding globulin (CBG) to amniotic fluid in the rabbit. *Endocrinology* 1989; **125:** 1321.

Smith CL, Hammond GL: Rat corticosteroid binding globulin: Primary structure and mRNA levels in the liver under different physiological conditions. *Mol Endocrinol* 1989; **3:** 420.

Thompson RT, Butland T, Marsh GM, Sprague C, Sanford SE, Driedger AA, Inch WR: An in vivo serial P-31 study of chronic cardiotoxicity induced by Adriamycin. *Proc Soc Magn Reson Med* 1989; **1:** 516.

Tuck AB, Chambers AF, Wilson SM: Expression of transfected *myc* or *ras* genes in murine LTA cells does not induce progression from a tumorigenic to a metastatic phenotype. *Proc Am Assoc Cancer Res* 1989; **30:** 386.

Underhill DA, Hammond GL: Organization of the human corticosteroid binding globulin gene and analysis of its 5' flanking region. *Mol Endocrinol* 1989; **3:** 1448.

Winger MJ, Macdonald DR, Cairncross JG: Supratentorial anaplastic glioma in adults—prognostic importance of extent of resection and prior low grade glioma. *J Neurosurg* 1989; **71:** 487.

Winger MJ, Macdonald DR, Schold SC, Cairncross JG: Selection bias in clinical trials of anaplastic glioma. *Ann Neurol* 1989; **26:** 531.

Xu J, Richardson C, Ford C, Spencer T, Li-juan Y, Mackie G, Hammond G, Possmayer F: Isolation and characterization of the cDNA for pulmonary surfactant-associated protein-B (SP-B) in the rabbit. *Biophys Biochem Res Commun* 1989; **160:** 325.

Yagel S, Khokha R, Denhardt DT, Kerbel RS, Parkar RS, Lala PK: Mechanisms of cellular invasiveness: A comparison of amnion invasion in vitro and metastatic behaviour in vivo. *J Natl Cancer Inst* 1989; **81:** 768.

Zochodne DW, Cairncross JG: Metastasis to the central nervous system. *In:* Kaiser H, ed. Cancer Growth and Progression—Metastasis/Dissemination. Dordrecht, The Netherlands: Kluwer Academic Publishers; 1989: 32.

OTTAWA

OCTRF Ottawa Regional Cancer Centre:

Benk V, Mazeron JJ, Grimard L, Martin M, Raynal M, Haddad E, Calitchi E, Pierquin B: Analyse retrospective des resultats de deux protocoles non randomises de traitment des T1 et T2 de la langue mobile. *Bull Cancer* 1988; **75:** 631.

Birnboim HC: A rapid alkaline extraction method for the isolation of plasmid DNA. *In:* Wu R, Grossman L, Moldave K, eds. Recombinant DNA Methodology. San Diego, CA: Academic Press Inc., 1989: 175 (Reprinted from 1983 article from Methods in Enzymology).

Birnboim HC, Doly J: A rapid alkaline extraction procedure for screening recombinant plasmid DNA. *Current Contents* 1988; **45:** 12. (Citation Classic)

Birnboim HC, Liteplo RG, Motora D: Indomethacin shifts peak of c-fos, egr-1, and c-myc gene expression in confluent fibroblasts induced by phorbol myristate acetate. *Biochem Biophys Res Commun* 1989; **161:** 508.

Burns BF, Cripps C, Dardick I: A case of Ki-1 large cell "anaplastic" lymphoma with ultrastructural features. *Hum Pathol* 1989; **4:** 393.

Capel B, Hawley RG, Covarrubias L, Hawley T, Mintz B: Clonal contributions of small numbers of retrovirally marked hematopoietic stem cells engrafted in unirradiated neonatal W/W^{v} mice. *Proc Natl Acad Sci* U S A. 1989; **86:** 4564.

Chammas S, Pater J, Mackillop W: An empirical approach to the definition of material information in ovarian cancer patients. *Clin Invest Med* 1989; **12:** (Abstract R-514).

Crook J, Esche B: Symposium: Brachytherapy. *Ann Roy Coll Physicians Surg Can* 1989; **22:** 351.

Danjoux CE, Gentner NE, Raaphorst P, Morrison DP: Lymphoblastic radiosensitivity in cancer patients. *Clin Invest Med* 1989; **12:** (Abstract R-493).

Eapen L, Stewart D, Danjoux C, Genest P, Futter N, Moors D, Irvine A, Crook J, Aitken S, Gerig L, Peterson R, Rasuli P: Intra-arterial cisplatin and concurrent radiation for locally advanced bladder cancer. *J Clin Oncol* 1989; **7:** 230.

Esche B, Crook J, Dutreix A, Wilson JF: Symposium: Brachytherapy. *Ann Roy Coll Physicians Surg Can* 1989; **22:** 351.

Evans WK: Supportive care for patients with small cell lung cancer. *J Int Assoc Study Lung Cancer* 1989; **5:** 319.

Evans WK, Wierzbicki R, Ayoub J, Cormier Y, Laberge F, Shepherd FA, Eisenhauer E: Amonafide (AMO) in previously untreated extensive small cell lung cancer (SCLC): Treatment results and lessons learned by the NCI Canada Clinical Trials Group. *Proc Am Soc Clin Oncol* 1989; **8:** 222. (Abstract 863)

Faddegon BA, Ross CK, Rogers DWO: Measurement of megavoltage *bremsstrahlung* spectra from linear accelerator. *Med Phys* 1989; **16:** 470. (Abstract)

Gerbaulet AP, Esche BA, Haie CM, Castaigne D, Flamant F, Chassagne D: Conservative treatment for lower gynecological tract malignancies in children and adolescents: The Institut Gustave-Roussy experience. *Int J Radiat Oncol Biol Phys* 1989; **17:** 655.

Girard A, Szantos J, Avruch L, Soubra M, Genest P: Magnetic resonance imaging for radiotherapy treatment planning. *Clin Invest Med* 1989; **12:** (Abstract R-528).

Grimard L, Mazeron JJ, Martin M, Raynal M, Marinello G, Pierquin B: Iridium-192 curietherapy alone for T1 and T2 carcinomas of the floor of the mouth. *Int J Radiat Biol Phys* 1989; **17:** 132. (Abstract 34)

Grimard L, Otmetzguine Y, Calitchi E, Despretz J, Pierquin B: A new approach in the conservative management of rectal cancer. *Clin Invest Med* 1989; **12:** (Abstract R-526).

Grimard L, Mazeron JJ, Marinello G, Pierquin B: Resultats locaux de l'endocurietherapie par iridium 192 des T1 et T2 du plancher buccal. *J Eur Radiother* 1989; **10:** 31.

Hawley RG, Sabourin LA, Hawley TS: An improved retrovital vector for gene transfer into undifferentiated cells. *Nucl Acids Res* 1989, **17:** 4001.

Hawley TS, Sabourin LA, Hawley RG: Comparative analysis of retroviral vector expression in mouse embryonal carcinoma cells. *Plasmid* 1989; **22:** 120.

Kanabus-Kaminska JM, Feeley M, Birnboim H: Simultaneous protective and damaging effects of cysteamine on intracellular DNA of leukocytes. *Free Radic Biol Med* 1988; **4:** 141.

Lishner M, Feld R, Sagman U, Sculier JP, Payne DG, Pringle JF, Yeoh JL, Evans WK, Shepherd FA, Maki E, Warr D: Late neurological complications after prophylactic cranial irradiation (PCI) in patients with small cell lung cancer (SCLC): The Toronto experience (1975-1985). *Proc Am Soc Clin Oncol* 1989; **8:** 22. (Abstract 870)

Liteplo RG: Altered methionine metabolism in metastatic variants of human melanoma cell line. *Cancer Lett* 1989; **44:** 23.

Liteplo RG, Hipwell SE: Agarose-selected variants of two human tumour cell lines exhibit altered methionine auxotrophy. *J Cell Physiol* 1989; **141:** 675.

Liteplo RG, Kerbel RS, Frost P: The contribution of DNA methylation to the generation of tumour cell heterogeneity, tumour progression and metastatis. *In:* Liotta L, ed. Cancer Growth and Progression, Vol. 3, Influence of Tumour Development. Dordrecht: Kluwer Academic Publisher; 1989: 103.

Lochrin C: Esthesioneuroblastoma. *Med Pediatr Oncol* 1989; **17:** 433.

Logan DM, Izaguirre CA, Kang C-Y: Establishment of long-term Kaposi's sarcoma-derived cell cultures from AIDS patients. *Proc Am Soc Clin Oncol* 1989; **8:** 4. (Abstract 14)

Maroun JA, Stewart DJ, Verma S, Eisenhauer E: Phase I study of Didemnin B given in a weekly schedule. *Proc Am Assoc Cancer Res* 1989; **30:** 284. (Abstract 1130)

Mazeron JJ, Chassagne D, Crook J, Bachelor F et al: Radiation therapy of carcinomas of the skin of nose and nasal vestibule: A report of 1676 cases by the Groupe Europeen de Curietherapie. *Radiol Oncol* 1989; **13:** 165.

Mazeron JJ, Crook J, Haddad E, Martin M, Peynegre R, Pierquin B: Irridium 192 implantation of squamous cell carcinoma of the oropharynx. *Am J Otolaryngol* 1989; **10:** 317.

Nair B, Joseph M, Catton G, Lach B: Radiation therapy in lymphomatoid granulomatosis. *Cancer* 1989; **64:** 821.

Otmezguine Y, Calitichi E, Despretz J, Grimard L, Feuilhade F, Brun B, Julien M, Le Bourgeois JP: A new combined approach in the conservative management of rectal cancer. *Proc Am Soc Clin Oncol* 1989; **8:** (Abstract 380).

Otmezguine Y, Grimard L, Calitichi E, Despretz J, Mazeron J, Le Bourgeois J, Pierquin B, Julien M: A new combined approach in the conservative management of rectal cancer. *Int J Radiat Oncol Biol Phys* 1989; **17:** 539.

Parliament M, Genest P, Girard A, Gerig L, Prefontaine M: Obstructive ureteropathy following radiation therapy for carcinoma of the cervix. *Gynecol Oncol* 1989; **33:** 237.

Perrault DJ, Aitken S: Managing your chemotherapy patient. *Perspect Geriatr* 1989; **5:** 29.

Pierquin B, Grimard L: Radiation therapy as primary treatment. *In:* Bloom HJG, ed. Breast Cancer (A UICC publication). Berlin: Springer-Verlag; 1989: 169.

Pierquin B, Marinello G, Grimard L: Normal tissue tolerance in the irradiation of the female breast. *In:* Vaeth JM, Meyer J, eds. Frontiers of Radiation Therapy and Oncology. Basel: S. Karger; 1989: 341.

Powe JE, Danjoux C, Blanchard R, Holmes R, McEwan S, Wahl R: Symposium: Radioisotope therapy in malignant disease. *Ann Roy Coll Physicians Surg Can* 1989; **22:** 353.

Raaphorst GP: Thermal radiosensitization in vitro. *In:* Urano M, ed. Hyperthermia and Oncology, vol. II. Utrecht, Holland: VSP; 1989: 17.

Raaphorst GP, Danjoux CE, Maroun J, Fisher B, Szekely J, Martin L, Feeley M: Combined cytotoxicity of lonidamine, radiation and hyperthermia in human tumour cells. *Proc Am Assoc Cancer Res* 1989; **30:** 147. (Abstract 2188)

Raaphorst GP, Feeley MM, Danjoux CE, Gerig LH, DaSilva V: Hyperthermia and radiation in repair of damage of human glioma cells. *Clin Invest Med* 1989; **12:** (Abstract R518).

Raaphorst GP, Feeley MM, DaSilva V, Danjoux CE, Gerig LH: A comparison of heat and radiation sensitivity of three human glioma cell lines. *Int J Radiat Oncol Biol Phys* 1989; **17:** 615.

Ripmeester JA, Ratcliffe CI, Cameron IG: Molecular motion in solid p-nitrophenol inlusion compounds of cyclomalto-hexose and -heptose (and Cyclodextrins): NMR and dielectric studies. *Carbohydrate Res* 1989; **192:** 69.

Shepherd FA, Evans WK, Feld R et al: Adjuvant chemotherapy following surgical resection for small cell carcinoma of the lung. *In:* Rogers, Desprez, Cline, eds. Yearbook of Medicine. Chicago, Illinois: Year Book Medical Publishers; 1989: 198.

Shepherd FA, Ginsburg RJ, Patterson GA, Evans WK, Feld R, University of Toronto Lung Oncology Group: A prospective study of adjuvant surgical resection after chemotherapy for limited small cell lung cancer. *J Thorac Cardiovasc Surg* 1989; **97:** 177.

Stewart DJ: Chemotherapy of malignant gliomas in adults. *Oncol Interchange* 1989; **3:** 1.

Stewart DJ: Pros and cons of intra-arterial chemotherapy. *Oncology* 1989; **3:** 20.

Stewart DJ: The role of chemotherapy in the treatment of gliomas in adults. *Cancer Treat Rev* 1989; **16:** 129.

Stewart DJ, Evans WK: Non-chemotherapeutic agents which potentiate chemotherapy efficacy. *Cancer Treat Rev* 1989; **16:** 1.

Stewart DJ, Maroun JA, Verma S, Perrault D, Earhart RH: Phase I study of weekly intravenous administration of menogaril to adults with solid tumors. *Am J Clin Oncol* 1989; **12:** 511.

Stewart DJ, Verma S, Maroun JA, Robillard L, Perrault DJ, Young V, Gupta S: Phase I study of idarubicin administered orally on a daily X 3 schedule. *Investig New Drugs*, 1989.

Szekely JG, Lobreau AU, Raaphorst GP, Feeley M: Morphological effects of lonidamine on human tumour cells. *J Scanning Microscopy* 1989; **3:** 681.

Szekely JG, Raaphorst GP, Lobreau AU, Einspenner M, Sargent MD, Azzam EI: The use of flow cytometry in radiation biology. Atomic Energy of Canada Ltd., AECL 10025, 1989.

Wilkins D, Raaphorst GP, Saunders JK: Magnetic resonance microimaging of 9L rat gliomas following radiotherapy. *Proc Soc Magnetic Res Med* 1989; **2:** 740.

Northeastern Ontario Oncology Program

Dohner H, Guckel F, Knauf W, Semmler W, van Kaick G, Ho AD et al: Magnetic resoncance imaging of bone marrow in lymphoproliferative disorders: Correlation with bone marrow biopsy. *Br J Haematol* 1989; **73:** 12.

Dunscombe PB: The teaching of physics and related courses to residents in radiation oncology. *Can Assoc Radiol J* 1989; **40:** 211.

Dunscombe PB, Cetas TC, Connor WG et al: Hyperthermia treatment planning: Report of Task Group no. 2 Hyperthermia Committee AAPM. New York: American Association of Physicists in Medicine, 1989: 59. (AAPM report; 27)

Dunscombe PB, Fox K: The precision of determining compliance with prescribed fields from conventional portal films. *Br J Radiol* 1989; **62:** 48.

Guckel F, Dohner H, Knauf W, Ho AD, Semmler W, van Kaick G: MR-tomographischer Nachweis von Knochenmarkinfiltration bei malignen Lymphomen. *Onkologie* 1989; **12(Suppl 1):** 34.

Guckel F, Semmler W, Dohner H, Knauf W, Gorich J, Ho AD et al: Kernspintomographische Darstellung von Knochenmarkinfiltrationen bei malignen Lymphomen. *Fortschr Rontgenstrahlen* 1989; **150:** 26.

Ho AD: Neue Wege einer an der Lebensqualitat orientierten ambulanten Krebstherapie: Ambulante Therapie am Beispiel der Hamoblastosen. *Aktuel Onkologie* 1989; **47:** 14.

Ho AD, Del Valle F, Ruckle H et al: Mitoxantrone and high-dose cytarabine as salvage therapy for refractory non-Hodgkin's lymphoma. *Cancer* 1989; **64:** 1388.

Ho AD, Ganeshaguru K, Knauf W et al: Enzyme activities of leukemic cells and biochemical changes induced by deoxycoformycin in vitro —lack of correlation with clinical response. *Leuk Res* 1989; **13:** 269.

Ho AD, Grossmann M, Knauf W et al: Plasma levels of soluble CD8 antigen and interleukin-2 receptor antigen in patients with hairy cell leukemia, relationship with splenectomy and with clinical response to therapy. *Leukemia* 1989; **3:** 718.

Ho AD, Thaler J, Mandelli F et al: Response to Pentostatin in hairy-cell leukemia refractory to interferon-alpha. *J Clin Oncol* 1989; **7:** 1533.

Korbling M, Hunstein W, Fliedner TM, Cayeux S, Dorken B, Fehrentz D, Haas R, Ho AD et al: Disease-free survival after autologous bone marrow transplantation in patients with acute myelogenous leukemia. *Blood* 1989; **74:** 1898.

Mannel DN, Kist A, Ho AD et al: Tumor necrosis factor production and natural killer cell activity in peripheral blood during treatment with recombinant tumour necrosis factor. *Br J Cancer* 1989; **60:** 585.

Mattern J, Efferth T, Bak M, Ho AD, Volm M: Detection of P-glycoprotein in human leukemias using monoclonal antibodies. *Blut* 1989; **58:** 215.

Thaler J, Denz H, Dietze O, Gastl G, Ho AD et al: Immunohistological assessment of bone marrow biopsies from patients with hairy cell leukemia: Changes following treatment with alpha-a-interferon and deoxycoformycin. *Leuk Res* 1989; **13:** 377.

Trumper LH, Ho AD, Hunstein W, van der Lelie H, Goudsmit R: Therapy of the myeloid blast phase of chronic granulocytic leukemia with plicamycin and hydroxyurea. *Blut* 1989; **58:** 85.

Vecsei P, Frank K, Haack D, Heinze V, Ho AD et al: Primary glucocorticoid receptor defect with likely familial involvement. *Cancer Res* 1989; **49:** 2220s.

Volm M, Efferth T, Bak M, Ho AD, Mattern J: Detection of the multidrug resistant phenotype in human tumours by monoclonal antibodies and the streptavidin-biotinylated phycoerythrin complex method. *Eur J Cancer Clin Oncol* 1989; **25:** 743.

Wiedenmann B, Reichardt P, Rath U, Theilmann L, Schule B, Ho AD et al: Phase-I trial of intravenous continuous infusion of tumor necrosis factor in advanced metastatic carcinomas. *J Cancer Res Clin Oncol* 1989; **115:** 189.

THUNDER BAY

OCTRF Thunder Bay Regional Cancer Centre:

McLean M: Primary management of limited laryngeal cancer by radiotherapy and surgical salvage: Results of 164 cases treated in district hospital. *Clin Oncol* 1989; **1:** 97.

Sellick SM: On specialty designation. *Alberta Psychol* 1988; **17:** 15.

Sellick SM: Training to criterion in biofeedback and migraine headaches. *Med Psychother* 1989; **2:** 115.

TORONTO

Ontario Cancer Institute

Adams F, Cruz L, Deachman MJ, Zamora E: Plaques may complicate subcutaneous opioid infusions. *J Nurs* 1989; **89:** 109.

Adams F, Cruz L, Deachman MJ, Zamora E: Focal subdermal toxicity with subcutaneous opioid infusion in patients with cancer pain. *J Pain Symptom Manage* 1989; **4:** 31.

Ahuja H, Bar-Eli M, Advani SH, Benchimol S, Cline MJ: Alterations in the p53 gene and the clonal evolution of the blast crisis of chronic myelocytic leukemia. *Proc Natl Acad Sci U S A* 1989; **86:** 6783.

Archer MC: Mechanisms of action of N-nitroso compounds. *Cancer Surv* 1989; **8:** 241.

Asch MR, Poon PY, McCallum RW, Bird BI: Myelolipoma: Radiologic findings in seven patients. *Can Assoc Radiol J* 1989; **40:** 247.

Barr J, Tannoch I: Analyzing the same data in two ways: A demonstration model to illustrate the reporting and misreporting of clinical trials. *J Clin Oncol* 1989; **7:** 969.

Bell RS, O'Sullivan B, Langer F, Mahoney JL, Lichtenstein SV, Moffat FL, Cummings BJ, Hawkins NV, Fornasier VL: Complications and functional results after limb-salvage surgery and radiotherapy for difficult mesenchymal neoplasms: A prospective analysis. *Can J Surg* 1989; **32:** 69.

Bell RS, O'Sullivan B, Liu FF, Powell J, Langer F, Fornasier VL, Cummings B, Miceli PN, Hawkins N, Quirt I et al: The surgical margin in soft-tissue sarcoma. *J Bone Joint Surg (Am)* 1989; **71:** 370.

Bell RS, Ready J, Hudson A, O'Sullivan B, Mahoney J, Richards R, Davis A, Fornasier VL: Non-neurogenic soft tissue tumours of the axilla: Prospective review of 16 cases. *J Surg Oncol* 1989; **42:** 73.

Benchimol S, Munroe DG, Rovinski B, Ben David Y, Bernstein A: Inactivation of the cellular p53 gene in friend virus-transformed erythroleukemia cell lines. *In:* Lohner H et al, eds. Vectors as Tools for the Study of Normal and Abnormal Growth and Differentation. NATO ASI Series, Vol. H34. Berlin: Springer-Verlag; 1989: 409.

Benchimol S, Munroe DG, Peacock J, Gray D, Smith LJ: Abnormalities in structure and expression of the p53 gene in leukemia. *Cancer Cells* 1989; **7:** 121.

Bergsagel DE: Is aggressive chemotherapy more effective in the treatment of plasma cell myeloma. *Eur J Cancer Clin Oncol* 1989; **25:** 159.

Bergsagel DE: Melphalan/prednisone versus drug combinations for plasma cell myeloma. *Eur J Haematol Suppl* 1989; **51:** 117.

Biondi A, Allavena P, Rossi V, Bassan R, Barbui T, Champagne E, Mak TW, Minden MD, Rambaldi A, Mantovani A: T cell receptor delta gene organization and expression in normal and leukemic natural killer cells. *J Immunol* 1989; **143:** 1009.

Biondi A, Champagne E, Rossi V, Giudici G, Cantu-Rajnoldi A, Masera G, Mantovani A, Mak TW, Minden MD: T-cell receptor delta gene rearrangement in childhood T-cell acute lymphoblastic leukemia. *Blood* 1989; **73:** 2133.

Biondi A, Norman C, Messner HA, Minden MD: Restriction fragment length polymorphism analysis of hematopoietic cells following successful treatment of relapsed acute lymphoblastic leukemia following bone marrow transplantation. *Bone Marrow Transplant* 1989; **4:** 705.

Biran H, Feld R, Sagman U, Rusthoven J, Shepherd FA, Evans WK, Ginsberg RJ, Panzarella T, Malkin A: Carcinoembryonic antigen, arginine vasopressin and calcitonin as markers of early small-cell lung cancer relapse. *Tumour Biol* 1989; **10:** 258.

Birek C, Patterson B, Maxymiw WG, Minden MD: EBV and HSV infection in a patient who had undergone bone marrow transplantation: Oral manifestations and diagnosis by in situ nucleic acid hybridization. *Oral Surg Oral Med Oral Pathol* 1989; **68:** 612.

Bird RP, McLellan E, Bruce WR: Aberrant crypts, putative precancerous lesions, in the study of the role of diet in the aetiology of colon cancer. *Cancer Surv* 1989; **8:** 189.

Bloch B, Soeters RP, Dehaeck CM, Levin W, Smith JA, Darge L: Tumour marker CA125 levels in a variety of benign and malignant conditions. *S Afr Med J* 1989; **76:** 670.

Boyd NF, McGuire V, Fishell E, Kuriov V, Lockwood G, Tritchler D: Plasma lipids in premenopausal women with mammographic dysplasia. *Br J Cancer* 1989; **59:** 766.

Bradley G, Naik M, Ling V: P-glycoprotein expression in multidrug-resistant human ovarian carcinoma cell lines. *Cancer Res* 1989; **49:** 2790.

Brandwein JM, Callum J, Sutcliffe SB, Rubinger M, Scott JG, Keating A: DHAP chemotherapy for relapsed Hodgkin's disease. *Proc Am Soc Clin Ocol* 1989, **8:** 265. (Abstract 1034)

Brandwein JM, Sutcliffe SB, Scott JG, Keating A: Cytoreductive salvage regimens in preparation for intensive therapy and autologous bone marrow transplantation. *Exp Hematol* 1989; **17:** 675. (Abstract 458)

Brandwein JM, Sutcliffe SB, Scott JG, Keating A: Salvage chemotherapy in preparation for intensive therapy and autologous bone marrow transplantation. *Clin Invest Med* 1989; **12:** B46. (Abstract R286)

Bristow RG, Wood RE, Clark GM: Thyroid dose distribution in dental radiography. *Oral Surg Oral Med Oral Pathol* 1989; **68:** 482.

Buick RN, Filmus J, Church J: Studies of EGF-mediated growth control and signal transduction using the MDA-MB-468 human breast cancer cell line. *In:* Ragaz J, ed. Effects of Therapy on Biology and Kinetics of Surviving Tumor. New York: Alan Liss Inc; 1989: 179.

Caccia N, Mak TW: Human T cell receptors. *Transplant Proc* 1989; **21:** 18.

Cairncross JG, Laperriere NJ: Low-grade glioma: To treat or not to treat. *Arch Neurol* 1989; **46:** 1238.

Champagne E, Takihara Y, Sagman U, De Sousa J, Burrow S, Lewis WH, Mak TW, Minden MD: The T-cell receptor delta chain locus is disrupted in the T-ALL associated t(11;14)(p13;q11) translocation. *Blood* 1989; **73:** 1672.

Chan A, Mak TW: Genomic organization of the T cell receptor. *Cancer Detect Prev* 1989; **14:** 261.

Chen JC, Hardy PA, Clauberg M, Joshi JG, Parravano J, Deck JH, Henkelman RM, Becker LE, Kucharczyk W: T2 values in the human brain: Comparison with quantitative assays of iron and ferritin. *Radiology* 1989; **173:** 521.

Church JG, Mills GB, Buick RN: Activation of the Na+/H+ antiport is not required for epidermal growth factor-dependent gene expression, growth inhibition or proliferation in human breast cancer cells. *Biochem J* 1989; **257:** 151.

Ciampi A, Lockwood G, Sutherland HJ, Llewellyn-Thomas HA, Till JE: Assessment of health-related quality of life: Factor scales for patients with breast cancer. *J Psychol Oncol* 1989; **6:** 1.

Cillo C, Ling V, Hill RP: Drug resistance in KHT fibrosarcoma cell lines with different metastatic ability. *Int J Cancer* 1989; **43:** 107.

Cillo C, Ling V, Hill RP: Gene amplification and tumor progression. *Pathol Biol (Paris)* 1989; **37:** 1032.

Claesson MH, Miller RG: Functional heterogeneity in allospecific cytotoxic T lymphocyte clones. III. Direct correlation between development of syngeneic cytotoxicity and loss of veto activity; implications for the mechanism of veto action. *Scand J Immunol* 1989; **29:** 493.

Clark RM, Chua T: Breast cancer and pregnancy: The ultimate challenge. *Clin Oncol (Roy Coll Radiol)* 1989; **1:** 11.

Constable RT, Kay I, Smith MR, Henkelman RM: High quality zoomed MR images. *J Comput Assist Tomogr* 1989; **13:** 179.

Cummings BJ: Influence of radiation therapy on cure and recurrence rates. *Cancer Surv* 1989; **8:** 49.

Cummings BJ: The treatment of anal cancer. *Int J Radiat Oncol Biol Phys* 1989; **17:** 1359.

Cummings BJ: Radiation therapy and rectal carcinoma. *Perspect Colon Rect Surg* 1989; **2:** 1.

Cunningham AJ, Tocco EK: A randomized trial of group psychoeducational therapy for cancer patients. *Patient Educ Couns* 1989; **14:** 101.

Cunningham JR: Dose calculations for high energy electron and photon beams. *Comput Med Imaging Graph* 1989; **13:** 241.

Cunningham JR: Development of computer algorithms for radiation treatment planning. *Int J Radiat Oncol Biol Phys* 1989; **16:** 1367.

Denekamp J, Whitmore GF, Jeggo P: Biphasic survival curves for XRS radiosensitive cells: Subpopulations or transient expression of repair competence. *Int J Radiat Biol Relat Stud Phys Chem Med* 1989; **55:** 605.

Deuchars KL, Ling V: P-glycoprotein and multidrug resistance in cancer chemotherapy. *Semin Oncol* 1989; **16:** 156.

Dulhanty AM, Li M, Whitmore GF: Isolation of Chinese hamster ovary cell mutants deficient in excision repair and mitomycin C bioactivation. *Cancer Res* 1989; **49:** 117.

El-Khatib EE, Evans M, Pla M, Cunningham JR: Evaluation of lung dose correction methods for photon irradiations of thorax phantoms. *Int J Radiat Oncol Biol Phys* 1989; **17:** 871.

Endicott JA, Ling V: The biochemistry of P-glycoprotein-mediated multidrug resistance. *Annu Rev Biochem* 1989; **58:** 137.

Feld R: Late complications associated with the treatment of small- cell lung cancer. *Cancer Treat Res* 1989; **45:** 301.

Feld R: Long term complications in small cell lung cancer. *In:* Hansen HH, ed. Basic and Clinical Concepts of Lung Cancer. Boston: Kluwer; 1989: 301.

Feld R: The compromised host. *Eur J Cancer Clin Oncol* 1989; **25:** S1.

Feld R: Quality of life assessment in patients with carcinoma of the lung. *Chest* 1989; **96:** 105S.

Feld R, Abeloff MD, Ball DL, Drings P, Gregor A, Johnson B, Maasilta P, Saijo N, Sorenson S, Van Zandwijk N: Toxicity and supportive care in small cell lung cancer: A consensus report. *Lung Cancer* 1989; **5:** 146.

Ferrick DA, Min X, Gajewski DA, Mak TW: Phenotypic analysis of mice transgenic for the TCR C gamma 4 (V gamma 1.1J gamma 4C gamma 4) gene. *Cold Spring Harb Symp Quant Biol* 1989; **54:** 57.

Ferrick DA, Ohashi PS, Wallace V, Schilham M, Mak TW: Thymic ontogeny and selection of alpha beta and gamma delta T cells. *Immunol Today* 1989; **10:** 403.

Ferrick DA, Sambhara SR, Ballhausen W, Iwamoto A, Pircher H, Walker CL, Yokoyama WM, Miller RG, Mak TW: T cell function and expression are dramatically altered in T cell receptor V gamma 1.1J gamma 4C gamma 4 transgenic mice. *Cell* 1989; **57:** 483.

Ferrick DA, Sambhara SR, Chadwick BS, Miller RG, Mak TW: The T-cell receptor repertoire is strikingly similar in older nude mice compared to normal adult mice. *Thymus* 1989; **13:** 103.

Fine S, Erlichman C, Kaizer L, Warr D, Elhakin T: An overview of 5-fluorouracil and high-dose leukovorin in the treatment of advanced carcinoma of the breast. *In:* Pinedo HM, Rustum YM, eds. Leukovorin modulation of fluoropyrimidines: A new frontier in cancer chemotherapy. New York: Royal Society of Medicine Services Ltd., 1989; **158:** 107.

Florence LS, Ito T, Ang KK, Jiang GL, Wong CS, Goto S, Didlake R, Kim EK, Stepkowski S, Kahan BD: The synergistic effect of total-lymphoid irradiation with extracted donor alloantigen in inducing transplantation unresponsiveness. *Transplantation* 1989; **47:** 156.

Foster FS, Larson JD, Mason MK, Shoup TS, Nelson G, Yoshida H: Development of a 12 element annular array transducer for realtime ultrasound imaging. *Ultrasound Med Biol* 1989; **15:** 649.

Foster FS, Larson JD, Pittaro RJ, Corl PD, Greenstein AP, Lum PK: A digital annular array prototype scanner for realtime ultrasound imaging. *Ultrasound Med Biol* 1989; **15:** 661.

Foxwell BM, Mackie A, Ling V, Ryffel B: Identification of the multidrug resistance-related P-glycoprotein as a cyclosporine binding protein. *Mol Pharmacol* 1989; **36:** 543.

Frederickson RM, Micheau MR, Iwamoto A, Miyamoto NG: 5' flanking and first intron sequences of the human B-actin gene required for efficient promoter activity. *Nucleic Acids Res* 1989; **17:** 253.

Gospodarowicz MK, Hawkins NV, Rawlings GA, Connolly JG, Jewett MA, Thomas GM, Herman JG, Garrett PG, Chua T, Duncan W et al: Radical radiotherapy for muscle invasive transitional cell carcinoma of the bladder: Failure analysis. *J Urol* 1989; **142:** 1448.

Gregoire RC, Stern HS, Yeung KS, Stadler J, Langley S, Furrer R, Bruce WR: Effect of calcium supplementation on mucosal cell proliferation in high risk patients for colon cancer. *Gut* 1989; **30:** 376.

Grenman R, Burk D, Virolainen E, Buick RN, Church J, Schwartz DR, Carey TE: Clonogenic cell assay for anchorage-dependent squamous carcinoma cell lines using limiting dilution. *Int J Cancer* 1989; **44:** 131.

Griesser H, Tkachuk D, Reis MD, Mak TW: Gene rearrangements and translocations in lymphoproliferative diseases. *Blood* 1989; **73:** 1402.

Grotepass F, Nortje CJ, Wood RE: Central haemangioma of the mandible arising during orthodontic therapy. *Am Soc Dent Child J* 1989; **56:** 62.

Hara J, Benedict SH, Champagne E, Mak TW, Minden M, Gelfand EW: Relationship between rearrangement and transcription of the T-cell receptor alpha, beta, and gamma genes in B-precursor acute lymphoblastic leukemia. *Blood* 1989; **73:** 500.

Hara J, Yumura-Yagi K, Tawa A, Ishihara S, Murata M, Terada N, Izumi Y, Champagne E, Takihara Y, Mak TW et al: Molecular analysis of acute undifferentiated leukemia: Two distinct subgroups at the DNA and RNA levels. *Blood* 1989; **74:** 1738.

Hardy PA, Henkelman RM: Transverse relaxation rate enhancement caused by magnetic particulates. *Magn Reson Imaging* 1989; **7:** 265.

Henkelman RM, McVeigh ER, Crawley AP, Kucharczyk W: Very slow inplane flow with gradient echo imaging. *Magn Reson Imaging* 1989; **7:** 383.

Hill RP, Gulyas S, Whitmore GF: Toxicity of RSU-1069 for KHT cells treated in vivo or in vitro: Evidence for a diffusible toxic product. *Int J Radiat Oncol Biol Phys* 1989; **16:** 1111.

Hill RP, Milas L: The proportion of stem cells in murine tumors. *Int J Radiat Oncol Biol Phys* 1989; **16:** 513.

Hill RP, Vaughan WP, McNally N: Tumor cell kinetics and cytogenetics: Commentary. *In:* Chapman JD, Peters LJ, Withers HR, eds. Prediction of Tumor Treatment Response. New York: Pergamon Press; 1989: 127.

Hirani-Hojatti S, Milligan JR, Kovnat A, Brown K, Archer MC: Activation of the c-Ha-ras-1 proto-oncogene by methylation in vitro with alpha-acetoxy-N-nitrosodimethylamine. *Mol Carcinog* 1989; **2:** 101.

Hue RP, Vaughan WP, McNally N: Tumor cell kinetics and cytogenetics: Commentary. *In:* Chapman JD, Peters LJ, Withers HR, eds. Prediction of Tumor Treatment Response. New York: Pergamon Press; 1989: 127.

Iscove N, Cunningham A, Osoba D, Till J: Research priorities in the psychosocial and behavioural aspects of cancer care. *Humane Med* 1989; **5:** 26.

Iscove NN, Shaw AR, Keller G: Net increase of pluripotential hematopoietic precursors in suspension culture in response to IL-1 and IL-3. *J Immunol* 1989; **142:** 2332.

Jiang GL, Ang KK, Thames HD, Wong CS, Wendt CD: Response of plateau-phase C3 10T1/2 cells to radiation and concurrent administration of bleomycin. *Radiat Res* 1989; **120:** 306.

Juranka PF, Zastawny RL, Ling V: P-glycoprotein: Multidrug-resistance and a superfamily of membrane-associated transport proteins. *Faseb J* 1989; **3:** 2583.

Kaizer L, Boyd NF, Kriukov V, Tritchler D: Fish consumption and breast cancer risk: An ecological study. *Nutr Cancer* 1989; **12:** 61.

Kamboj RK, Gariepy J, Siu CH: Identification of an octapeptide involved in homophilic interaction of the cell adhesion molecule gp80 of dictyostelium discoideum. *Cell* 1989; **59:** 615.

Kartner N, Ling V: Multidrug resistance in cancer. *Sci Am* 1989; **260:** 44.

Keane TJ, Van Dyk J: TBI schedules prior to bone marrow transplantation: Requirements for comparison. *Radiother Oncol* 1989; **15:** 207.

Keating A, Brandwein JM, Sutcliffe SB, Scott JG: Etoposide, melphalan + total body irradiation: A novel, safe and effective autologous bone marrow transplant regimen for hematologic malignancies. *Exp Hematol* 1989; **17:** 721. (Abstract 559)

Keating A, Rubinger M, Sutcliffe SB, Scott JG: High dose etoposide, melphalan, total body irradiation and ABMT in patients with hematologic malignancies. *In:* Dicke KA, Spitzer G, Jagannath S, eds. Autologus Bone Marrow Transplantation: Proceedings of the Fourth International Symposium. Houston: The University of Texas M. D. Anderson Hospital and Tumor Institute; 1989: 101.

Kersey P, Kriukov V, Shannon P, Boyd NF: Cyclical mastopathy: An evaluation of methods of assessment. *J Clin Epidemiol* 1989; **42:** 53.

Klastersky J, Feld R, Kleisbauer JP, Rocmans P: Treatment of N2 non-small cell lung cancer (NSCLC). *Chest* 1989; **96:** 83S.

Kondo T, Kono H, Miyamoto N, Yoshida R, Toki H, Matsumoto I, Hara M, Inoue H, Inatsuki A, Funatsu T et al: Age- and sex-specific cumulative rate and risk of ATLL for HTLV-I carriers. *Int J Cancer* 1989; **43:** 1061.

Korycka BM, Hill RP: Dynamic heterogeneity: Experimental metastasis studies with RIF-1 fibrosarcoma. *Clin Exp Metastasis* 1989; **7:** 107.

Laing EJ, Fitzpatrick PJ, Binnington AG, Norris AM, Mosseri A, Rider WD, Valli VE, Baur A: Half-body radiotherapy in the treatment of canine lymphoma. *J Vet Intern Med* 1989; **3:** 102.

Laing EJ, Fitzpatrick PJ, Norris AM, Mosseri A, Rider WD, Binnington AG, Baur A, Valli VE: Half-body radiotherapy: Evaluation of the technique in normal dogs. *J Vet Intern Med* 1989; **3:** 96.

Lamers MC, Vakil M, Kearney JF, Langhorne J, Paige CJ, Julius MH, Mossmann H, Carsetti R, Kohler G: Immune status of a mu, kappa transgenic mouse line: Deficient response to bacterially related antigens. *Eur J Immunol* 1989; **19:** 459.

Langley GR, Till JE: Exemplary family physicians and consultants: Empirical definition of contemporary medical practice. *Can Med Assoc J* 1989; **141:** 301.

Lee C, Biondi A, Wang XH, Iscove NN, De Sousa J, Aarden LA, Wong GG, Clarke SC, Messner HA, Minden MD: A possible autocrine role for interleukin 6 in two lymphoma cell lines. *Blood* 1989; **74:** 798.

Lee-Han H, McGuire V, Boyd NF: A review of the methods used by studies of dietary measurement. *J Clin Epidemiol* 1989; **42:** 269.

Leung S, Miyamoto NG: Point mutational analysis of the human c-fos serum response factor binding site. *Nucleic Acid Res* 1989; **17:** 1171.

Lieberman DM, Reithmeier RA, Ling V, Charuk JH, Goldberg H, Skorecki KL: Identification of P-glycoprotein in renal brush border membranes. *Biochem Biophys Res Commun* 1989; **162:** 244.

Ling V: Does P-glycoprotein predict response to chemotherapy. *J Natl Cancer Inst* 1989; **81:** 84. (Editorial)

Ling V: Colchicine and colcemid in drug resistance in mammalian cells. *In:* Gupta RS, ed. Anticancer and Other Drugs; vol 2. Boca Raton, Florida: CRC Press; 1989: 139.

Lishner M, Curtis JE: Aplastic anaemia following successful treatment of malignant epithelial tumours with radiation and/or chemotherapy. *Br J Haematol* 1989; **73:** 416.

Lishner M, Curtis JE, Minkin S, McCulloch EA: Interaction between retinoic acid and cytosine arabinoside affecting the blast cells of acute myeloblastic leukemia. *Leukemia* 1989; **3:** 784.

Lishner M, Feld R, Sagman U, Sculier JP, Payne DG, Pringle JF, Yeoh JL, Evans WK, Shepherd FA, Make D, Warr D: Late neurological complications after prophylactic cranial irradiation (PCI) in patients (PTS) with small cell lung cancer (SCLC): The Toronto experience (1975-1985). *Proc Am Soc Clin Oncol* 1989; **8:** 224. (Abstract 870)

Lister TA, Crowther D, Sutcliffe SB, Glatstein E, Canellos GP, Young RC, Rosenberg SA, Coltman CA, Tubiana M: Report of a committee convened to discuss the evaluation and staging of patients with Hodgkin's disease: Cotswolds meeting (published erratum appears in J Clin Oncol 1990 Sep;8(9):1602). *J Clin Oncol* 1989; **7:** 1630.

Llewellyn-Thomas HA, Sims-Jones N, Sutherland HJ: Measuring perceptions of the exemplary nurse. *J Nurs Educ* 1989; **28:** 366.

Llewellyn-Thomas HA, Thiel EC, Clark RM: Patients versus surrogates: Whose opinion counts on ethics review panels. *Clin Res* 1989; **37:** 501.

Lockwood GR, Foster FS, Hunt JW: A ray tracing method for calculating the speed of sound in a nonparallel layered model using pulse echo ultrasound. *Ultrason Imaging* 1989; **11:** 106.

Luk CK, Tannock IF: Flow cytometric analysis of doxorubicin accumulation in cells from human and rodent cell lines. *J Natl Cancer Inst* 1989; **81:** 55.

Maki E, McDunnough P: Sampling a branching tree. *Stochastic Processes Applications* 1989; **31:** 283.

Maki E, McDunnough P: What can or can't be estimated in branching and related processes? *Stochastic Processes Applications* 1989; **31:** 307.

Mandell LA, Bergeron MG, Ronald AR, Vega C, Harding G, Saginur R, Feld R, Duperval R, Landis SJ, Miedzinski LJ et al: Once-daily therapy with ceftriaxone compared with daily multiple-dose therapy with cefotaxime for serious bacterial infections: A randomized, double-blind study. *J Infect Dis* 1989; **160:** 433.

Marshall RS, Paterson MC, Rauth AM: Deficient activation by a human cell strain leads to mitomycin resistance under aerobic but not hypoxic conditions. *Br J Cancer* 1989; **59:** 341.

Martin AJ, Drake JM, Lemaire C, Henkelman RM: Cerebrospinal fluid shunts: Flow measurements with MR imaging. *Radiology* 1989; **173:** 243.

Martin DR, Miller RG: In vivo administration of histoincompatible lymphocytes leads to rapid functional deletion of cytotoxic T lymphocyte precursors. *J Exp Med* 1989; **170:** 679.

Maxymiw WG, Wood RE: The role of dentistry in head and neck radiation therapy. *Can Dent Assoc J* 1989; **55:** 193.

Maxymiw WG, Wood RE: The role of dentistry in patients undergoing bone marrow transplantation. *Br Dent J* 1989; **167:** 229.

Maxymiw G, Wood RE, Anderson JD: The immediate role of the dentist in the maxillectomy patient. *J Otolaryngol* 1989; **18:** 303.

Messner HA: Experimental basis of antileukaemic chemotherapy. *Bone Marrow Transplant* 1989; **4:** 20.

Miauchi J, Kelleher CA, Wang C, Minkin A, McCulloch EA: Growth factors influence the sensitivity of leukemic stem cells to cytosine arabinoside in culture. *Blood* 1989; **73:** 1271.

Miller AB, Howe GR, Sherman GJ, Lindsay JP, Yaffe MJ, Dinner PJ, Risch HA, Preston DL: Mortality from breast cancer after irradiation during fluoroscopic examinations in patients being treated for tuberculosis. *N Engl J Med* 1989; **321:** 1285.

Miller RG, Martin DR: Veto in vivo. *Plzen Lek Sborn* 1989; **57(Suppl):** 27.

Miller RG, Martin DR, Teh HS, Kiziroglu F, Sambhara S: Role of the veto phenomenon in vivo. *In:* Melchers F et al, eds. Progress in Immunology VII. Berlin: Springer-Verlag; 1989: 861.

Miller N, McPherson K, Jones L, Vessey M: Histopathology of breast cancer in young women in relation to use of oral contraceptives. *J Clin Pathol* 1989; **42:** 387.

Milligan JR, Hirani-Hojatti S, Catz-Biro L, Archer MC: Methylation of DNA by three N-nitroso compounds: Evidence for sequence specific methylation by a common intermediate. *Chem Biol Interact* 1989; **72:** 175.

Minkin S: Fit assessment and identification of functional form in logistic regression. *Appl Statistics* 1989; **38:** 343.

Minkin S: Computing confidence intervals in GLIM. *In:* Decarli A, Francis BJ, Gilchrist R, Seeber GUH, eds. Statistical Modelling. Lecture Notes in Statistics No 57. New York: Springer-Verlag; 1989: 234.

Mitchell SA: A young man decides to live. *Coll Nurses Ont Communique* 1989; **November:** 1.

Miyauchi J, Kelleher CA, Wang C, Minkin S, McCulloch EA: Growth factors influence the sensitivity of leukemic stem cells to cytosine arabinoside in culture. *Blood* 1989; **73:** 1272.

Munro P, Rawlinson JA: A digital fluoroscopic imaging system for radiotherapy localization. *In:* Medical Imaging III: Image and Formation. SPIE 1989; **1090:** 321.

Neal MJ, Cunningham JR, Shah MA, Yazulla S: Immunocytochemical evidence that vigabatrin in rats causes GABA accumulation in glial cells of the retina. *Neurosci Lett* 1989; **98:** 29.

Newell KJ, Tannock IF: Reduction of intracellular pH as a possible mechanism for killing cells in acidic regions of solid tumors: Effects of carbonylcyanide-3-chlorophenylhydrazone. *Cancer Res* 1989; **49:** 4477.

Ng WF, Sarangi F, Zastawny RL, Veinot-Drebot L, Ling V: Identification of members of the P-glycoprotein multigene family. *Mol Cell Biol* 1989; **9:** 1224.

Nishikawa RM, Yaffe MJ, Holmes RB: Effect of finite phosphor thickness on detective quantum efficiency. *Med Phys* 1989; **16:** 773.

Noss MB, Panicucci R, McClelland RA, Rauth AM: 1-methyl-2-nitrosoimidazole: Cytotoxic and glutathione depleting capabilities. *Int J Radiat Oncol Biol Phys* 1989; **16:** 1015.

O'Sullivan K, Cunningham AJ: Intraoperative cerebral ischaemia. *Br J Hosp Med* 1989; **42:** 286.

Paige CJ, Wu GE: The B cell repertoire. *FASEB J* 1989; **3:** 1818.

Panicucci R, Heal R, Laderoute K, Cowan D, McClelland RA, Rauth AM: NLP-1: A DNA intercalating hypoxic cell radiosensitizer and cytotoxin. *Int J Radiat Oncol Biol Phys* 1989; **16:** 1039.

Pavlin CJ, Japp B, Simpson ER, McGowan HD, Fitzpatrick PJ: Ultrasound determination of the relationship of radioactive plaques to the base of choroidal melanomas. *Ophthalmology* 1989; **96:** 538.

Payne DG, Arriagada R, Dombernowsky P: The role of thoracic radiation therapy in small cell carcinoma of the lung. *In:* Hansen HH, Kristjansen PEG, eds. Management of Small Cell Lung Cancer. New York: Elsevier; 1989: 17.

Payne DG, Arriagada R, Dombernowsky P, Evans WK, Giaccone G, Holsti LR, Johnson D, McVie G, Sculier JP, Smyth J: The role of thoracic radiation therapy in small cell carcinoma of the lung. *Lung Cancer* 1989; **5:** 135.

Payne DG, Ginsberg RJ: Radiation therapy is indicated for asymptomatic inoperable lung cancer. *In:* Debates in Medicine. Year Book Medical Publishers Series 1989; **2:** 251.

Pircher H, Mak TW, Lang R, Ballhausen W, Ruedi E, Hengartner H, Zinkernagel RM, Burki K: T cell tolerance to Mlsa encoded antigens in T cell receptor V beta 8.1 chain transgenic mice. *Embo J* 1989; **8:** 719.

Poon CS, Szumowski J, Plewes DB, Ashby P, Henkelman RM: Fat/water quantitation and differential relaxation time measurement using chemical shift imaging technique. *Magn Reson Imaging* 1989; **7:** 369.

Reis MD, Griesser H, Mak TW: T cell receptor and immunoglobulin gene rearrangements in lymphoproliferative disorders. *Adv Cancer Res* 1989; **52:** 45.

Rothenberg M, Ling V: Multidrug resistance: Molecular biology and clinical relevance. *J Natl Cancer Inst* 1989; **81:** 907.

Ruckdeschel JC, Piantadosi S, Feld R: Assessment of quality of life (QL) by the functional living index-cancer (FLIC) is superior to performance status for prediction of survival in patients with lung cancer. *Proc Am Soc Clin Oncol* 1989; **8:** 311. (Abstract A1209)

Ruffie P, Feld R, Minkin S, Cormier Y, Boutan-Laroze A, Ginsberg R, Ayoub J, Shepherd FA, Evans WK, Figueredo A et al: Diffuse malignant mesothelioma of the pleura in Ontario and Quebec: A retrospective study of 332 patients. *J Clin Oncol* 1989; **7:** 1157.

Sagman U: Small cell lung cancer complications: Late toxicity. *Lung Cancer* 1989; **5:** 311.

Santyr GE, Henkelman RM, Bronskill MJ: Spin locking for magnetic resonance imaging with application to human breast. *Magn Reson Med* 1989; **12:** 25.

Sealy R, Jacobs P, Wood L, Levin W, Barry L, Boniaszczuk J, Blekkenhorst G: The treatment of tumors by the induction of anemia and irradiation in hyperbaric oxygen. *Cancer* 1989; **64:** 646.

Segal S, Feld R, Kurtz AB: Ultrasound case of the day: Ovarian fibroma. *Radiographics* 1989; **9:** 959.

Sheehy MJ, Meske LM, Emler CA, Rowe JR, Neme De Gimenez MH, Ingle CA, Chan A, Trucco M, Mak TW: Allelic T-cell receptor alpha complexes have little or no influence on susceptibility to type 1 diabetes. *Hum Immunol* 1989; **26:** 261.

Shepherd FA, Feld R, Blackstein M, Gupta S, Cook DJ, Lassus M: Administration of high dose bolus epirubicin (EPI) is not associated with increased cardiotoxicity. *Proc Am Soc Clin Oncol* 1989; **8:** 335. (Abstract A1304)

Sherar MD, Foster FS: The design and fabrication of high frequency poly(vinylidene fluoride) transducers (published erratum appears in Ultrason Imaging 1989 Oct;11(4):306-7). *Ultrason Imaging* 1989; **11:** 75.

Sherar MD, Starkoski BG, Taylor WB, Foster FS: A 100 MHz B-scan ultrasound backscatter microscope. *Ultrason Imaging* 1989; **11:** 95.

Simpson WJ: Invasive thymoma. *In:* Vincent F, ed. Symposium on Thymic Tumours. Basel, Switzerland: S. Karger; 1989: 147.

Simpson WJ: Unresectable thymoma. *In:* Vincent F, ed. Symposium on Thymic Tumours. Basel, Switzerland: S. Karger; 1989: 152.

Simpson WJ, Sutcliffe SB, Gospodarowicz MK: Thyroid cancer. *In:* Moss WT, Cox J, eds. Radiation Oncology, 6th ed. Saint Louis, MO: C.V. Mosby; 1989: 254.

Smith JT, Goodman SB, Fornasier VL: The histology of a failed shelf procedure. *Orthop Rev* 1989; **18:** 1069.

Soeters R, Bloch B, Levin W, Dehaeck CM, Goldberg G: Combined chemotherapy and radiotherapy in patients with advanced squamous carcinoma of the cervix (cis-platinum-bleomycin-vinblastine). *Gynecol Oncol* 1989; **33:** 44.

Soeters R, Levin W, Tiltman A, Bloch B, Dehaeck CM: A clinical appraisal of stage 1 mucinous carcinoma of the ovary. *Gynecol Oncol* 1989; **33:** 222.

Soeters R, Tiltman A, Learmonth G, Bloch B, Dehaeck K, Levin W: Peutz-Jeghers syndrome in association with adenoma malignum (minimal deviation adenocarcinoma) of the cervix: Case report. *Br J Obstet Gynaecol* 1989; **96:** 1101.

Sutcliffe SB: Hodgkin's disease. Chemotherapy. *In:* Rakel RE, ed. Conn's Current Therapy. Philadelphia: WB Sauders Co.; 1989: 343.

Sutherland HJ, Llewellyn-Thomas HA, Lockwood GA, Tritchler DL, Till JE: Cancer patients: Their desire for information and participation in treatment decisions. *J Roy Soc Med* 1989; **82:** 260.

Sutherland HJ, Lockwood GA, Minkin S, Tritchler DL, Till JE, Llewellyn-Thomas HA: Measuring satisfaction with health care: A comparison of single with paired rating strategies. *Soc Sci Med* 1989; **28:** 53.

Sutherland HJ, Lockwood GA, Cunningham AJ: A simple, rapid method for assessing psychological distress in cancer patients: Evidence of validity for linear analogue scales. *J Psychosoc Oncol* 1989; **7:** 31.

Takadera T, Leung S, Gernone A, Koga Y, Takihara Y, Miyamoto NG, Mak TW: Structure of the two promoters of the human lck gene: Differential accumulation of two classes of lck transcripts in T cells. *Mol Cell Biol* 1989; **9:** 2173.

Takihara Y, Champagne E, Ciccone E, Moretta L, Minden M, Mak TW: Organization and orientation of a human T cell receptor delta chain V gene segment that suggests an inversion mechanism is utilized in its rearrangement. *Eur J Immunol* 1989; **19:** 571.

Takihara Y, Reimann J, Michalopoulos E, Ciccone E, Moretta L, Mak TW: Diversity and structure of human T cell receptor delta chain genes in peripheral blood gamma/delta-bearing T lymphocytes. *J Exp Med* 1989; **169:** 393.

Tannock I, Gospodarowicz M, Connolly J, Jewett M: M-VAC (methotrexate, vinblastine, doxorubicin and cisplatin) chemotherapy for transitional cell carcinoma: The Princess Margaret Hospital experience. *J Urol* 1989; **142:** 289.

Tannock I, Gospodarowicz M, Meakin W, Panzarella T, Stewart L, Rider W: Treatment of metastatic prostatic cancer with low-dose prednisone: Evaluation of pain and quality of life as pragmatic indices of response. *J Clin Oncol* 1989; **7:** 590.

Tannock IF: Combined modality treatment with radiotherapy and chemotherapy. *Radiother Oncol* 1989; **16:** 83.

Tannock IF, Rotin D: Acid pH in tumors and its potential for therapeutic exploitation. *Cancer Res* 1989; **49:** 4373.

Tudek B, Bird RP, Bruce WR: Foci of aberrant crypts in the colons of mice and rats exposed to carcinogens associated with foods. *Cancer Res* 1989; **49:** 1236.

Turnbull DH, Wilson SR, Hine AL, Foster FS: Ultrasonic characterization of selected renal tissues. *Ultrasound Med Biol* 1989; **15:** 241.

Tweeddale M, Jamal N, Nguyen A, Wang XH, Minden MD, Messner HA: Production of growth factors by malignant lymphoma cell lines. *Blood* 1989; **74:** 572.

Van der Vliet W, Erlichman C, Elhakim T: Allopurinol mouthwash for prevention of fluorouracil-induced stomatitis. *Clin Pharm* 1989; **8:** 655.

Van Dyk J, Keane TJ: Determination of parameters for the linear-quadratic model for radiation-induced lung damage. *Int J Radiat Oncol Biol Phys* 1989; **17:** 695. (Letter)

Van Dyk J, Mah K, Keane TJ: Radiation-induced lung damage: Dose-time-fractionation considerations. *Radiother Oncol* 1989; **14:** 55.

Van Dyk J, Mah K, Keane TJ: Is there an influence of overall treatment time in the response of lung to fractionated radiotherapy? *Radiother Oncol* 1989; **14:** 169. (Letter)

Wandl U, Messner HA: Rapid decline of clonogenic hemopoietic progenitors in semisolid cultures of bone marrow samples derived from patients with chronic myeloid leukemia. *Int J Cell Cloning* 1989; **7:** 314.

Wang C, Curtis JE, Geissler EN, McCulloch EA, Minden MD: The expression of the proto-oncogene C-kit in the blast cells of acute myeloblastic leukemia. *Leukemia* 1989; **3:** 699.

Wang C, Curtis JE, Minden MD, McCulloch EA: Expression of a retinoic acid receptor gene in myeloid leukemia cells. *Leukemia* 1989; **3:** 264.

Whitmore GF, Varghese AJ, Gulyas S. Cell cycle responses of two X-ray sensitive mutants defective in DNA repair. *Int J Radiat Biol* 1989; **56:** 657.

Wong CS, Ang KK, Fletcher GH, Thames HD, Peters LJ, Byers RM, Oswald MJ: Definitive radiotherapy for squamous cell carcinoma of the tonsillar fossa. *Int J Radiat Oncol Biol Phys* 1989; **16:** 657.

Wood RE, Bristow R, Clark GM, Nussbaum C, Taylor KW: A technique-dependent decrease in thyroid absorbed dose with higher kilovoltage complete-mouth dental radiographic procedures. *Health Phys* 1989; **56:** 893.

Wood RE, Nortje CJ: General practitioner's radiology casebook: Ameloblastoma. *J Dent Assoc S Afr* 1989; **44:** 18.

Yaffe MJ: The medi-drama as an instrument to teach doctor-patient relationships. *Med Teach* 1989; **11:** 321.

Yee C, Biondi A, Wang XH, Iscove NN, De Sousa J, Aarden LA, Wong GG, Clark SC, Messner HA, Minden MD: A possible autocrine role for interleukin-6 in two lymphoma cell lines. *Blood* 1989; **74:** 798.

Young SD, Hill RP: Radiation sensitivity of tumour cells stained in vitro or in vivo with the bisbenzimide fluorochrome Hoechst 33342. *Br J Cancer* 1989; **60:** 715.

Yumura-Yagi K, Hara J, Terada N, Ishihara S, Tawa A, Takihara Y, Champagne E, Minden MD, Mak TW, Kawa-Ha K: Analysis of molecular events in leukemic cells arrested at an early stage of T-cell differentiation. *Blood* 1989; **74:** 2103.

OCTRF Toronto-Bayview Regional Cancer Centre:

Ackerman I, Dembo A: An update of prognostic factors in gynecological cancer. *Curr Opin Oncol* 1989; **1:** 82.

Anderson RA, Doyle J, Weitzman S, Jenkin RDT, Greenberg ML: Persistent mediastinal masses in Hodgkin's disease (HD) in childhood. *Proc Am Soc Clin Oncol* 1989; **8:** 279. (Abstract 1070)

Balogh J, Sutherland S: Osteoradionecrosis of the mandible, a review. *J Otolaryngol* 1989; **18:** 245.

Berinstein N, Levy R: Activation of an excluded immunoglobulin allele in a human B lymphoma cell line. *Science* 1989; **244:** 337.

Covens A, Jamieson C, Thomas G, De Petrillo A: Surgical management of radiation induced bowel injury as a treatment of cervical carcinoma. *Can J Surg* 1989; **32:** 304. (Abstract)

Davey P: Radiobiology: nil desperandum. *Br J Hosp Med* 1989; **42:** 206.

Doyle JJ, Greenberg ML, Jenkin RDT: Comparison of combined modality therapy *vs* chemotherapy alone for the treatment of Hodgkin's disease. *Pediatr Res* 1989; **25:** 150A.

Iscoe N, Cunningham A, Osoba D, Toll J: Psychosocial issues in patients with cancer: A group consensus approach. *Humane Med* 1989; **5:** 26.

Iscoe N, Hume S: Methodology guidelines for reporting studies in malignant melanoma: Late referral bias. *Proc Am Soc Clin Oncol* 1989; **8:** 282. (Abstract 1100)

Jenkin D, Goddard K, Armstrong D, Becker L, Berry M, Chan H, Doherty M, Greenberg M, Hendrick B, Hoffman H, Humphrey R, Weitzman S, Zipursky A: Medulloblastoma in children: Current prognostic factors. *Int J Radiat Oncol Biol Phys* 1989; **17:** 137. (Abstract)

Jenkin D, Goddard K, Armstrong D, Berry M, Chan H, Doherty M, Greenberg M, Hendrick B, Hoffman H, Humphrey R, Weitzman S, Zipursky A: Medulloblastoma: A re-evaluation of multimodality treatment. *Proc Am Soc Clin Oncol* 1989; **8:** 302. (Abstract 1177)

Lassam N, Jay G: Suppression of MHC class I RNA in highly oncogenic cells occurs at the level of transcription initiation. *Immunology* 1989; **143:** 3792.

Marks A, Buckman R, Kwok CS et al: Preclinical and clinical studies of radioiodinated monoclonal antibody 2G3 for therapy of intraperitoneal effusions associated with carcinoma of breast and ovary. *Antibody Immunoconjug Radiophermaceut* 1989; **2:** 83.

Meadows AT, Sposto R, Jenkin RDT, Kersey JH, Chilcote RR, Siegel SE, Coccia PF, Rosenstock HM, Pringle KC, Stolar CJ, Kadin ME, Hammond GD: Similar efficacy of 6 and 18 months of therapy with four drugs (COMP) for localized non-Hodgkin's lymphoma of children: A report from the Children's Cancer Study Group. *J Clin Oncol* 1989; **7:** 92.

O'Brien PF, Farraday L: A head swivel technique for breast tangents. *Med Dosimetry* 1989; **14:** 113.

Pritchard KI: Chemotherapy and endocrine therapy in metastatic disease. *In:* Abeloff M, ed. Current Opinion in Oncology. Philadelphia: Current Science Publishing; 1989: 324.

Pritchard KI: Screening for endometrial cancer: Is it effective? *Ann Intern Med* 1989; **110:** 177. (Editorial)

Pritchard KI: Systemic adjuvant therapy for node negative breast cancer: Proven or premature? *Ann Intern Med* 1989; **111:** 1. (Editorial)

Pritchard KI, Buckman RA, Sutherland DJA, MacKenzie RG, Ackerman I, Doherty M, Catton P: Adjuvant therapy for node negative breast cancer. *N Engl J Med* 1989; **321:** 471. (Letter)

Pritchard KI, Pater J, Paul N, Paterson AHG, Fine S: Thromboembolic complications related to chemotherapy in a National Cancer Institute of Canada (NCI-C) randomized trial of tamoxifen (T) *vs* T plus chemotherapy in postmenopausal women with axillary node positive receptor positive breast cancer. *Proc Am Soc Clin Oncol* 1989; **8:** 25. (Abstract 92)

Pritchard KI, Sutherland DJA: Therapy of advanced breast cancer: The use of endocrine therapy. *In:* Henderson IC, ed. Hematology Oncology Clinics of North America. Philadelphia: U.B. Saunders Co.; 1989: 765.

Sawka CA: A decision analysis (DA) of treatment strategies for pathological Stages I and II Hodgkin's disease (HD). *Proc Am Soc Clin Oncol* 1989; **8:** 273. (Abstract 1066)

Sposto R, Ertel I, Jenkin RDT, Boesel C, Venes J, Ortega J, Evans A, Wara W, Hammond D: The effectiveness of chemotherapy for treatment of high grade astrocytoma in children: Results of a randomized trial. *J Neurooncol* 1989; **7:** 165.

Thomas G: Optimizing therapy in bulky Stage II seminoma. *In:* Johnson D, Logothetis C, von Eschenbach A, eds. Systemic Therapy for Genitourinary Cancer. Chicago: Year Book Medical Publishers; 1989: 298. Chicago

Thomas G: Radiation therapy. *In:* Berek JS, Hacker NF, eds. Practical Gynecology Oncology. Baltimore: Williams & Wilkins; 1989: 37.

Thomas G, Dembo A, De Petrillo A, Pringle J, Ackerman I, Bryson P, Balogh J, Osborne R, Rosen B, Fyles A: Concurrent radiation and chemotherapy in vular carcinoma. *Gynecol Oncol* 1989; **34:** 263.

Thomas G, Sturgeon JF, Allison R, Jewett M, Goldberg S, Sugar L, Rideout D, Gospodarowicz M: A study of post-orchidectomy surveillance in Stage I testicular seminoma. *J Urol* 1989; **142:** 313.

OCTRF Corporate Office:

Clarke EA: Cervical cancer screening: The time for reappraisal. *Can J Public Health* 1988; **79:** 277. (Letter)

Clarke EA: National Council of Cancer Registries. *Chronic Dis Can* 1988; **9:** 51.

Clarke EA: Ontario screening program for breast cancer. *ONCORE* 1989; **1:** 6.

Clarke EA, Anderson TW: Does screening by "Pap" smear help prevent cervical cancer? *In:* Buck C, Llopis A, Najera E, Terris M, eds. The Challenge of Epidemiology: Issues and Selected Readings. PanAmerican Health Organization Scientific Publication No. 505. Washington, D.C.: World Health Organization; 1988: 888.

Clarke EA, Marrett LD, Kreiger N: Cancer registration in Ontario: A computer approach to cancer registration. *In:* Jensen OM, Parkin DM et al, eds. Cancer Registration: Principles and Methods. Lyon: IARC Scientific Publications; 1989: No. 95.

Boice J, ..., Kreiger N et al: Radiation dose and breast cancer risk in patients treated for cancer of the cervix. *Int J Cancer* 1989; **44:** 7.

Heath C, Kagey B, Kanarek M, Mandel J, Marrett L, Stark A, VanOostdem J, Vena J: Report of work group on epidemiology at the workshop to evaluate risks to human health associated with exposure to toxic chemicals in the Great Lakes basin ecosystem. Niagara-on-the-Lake, Ontario, April, 16-18, 1989. *In:* Flint RW, Vena JE, eds. Evaluating Risks to Human Health Associated with Exposure to Toxic Chemicals in the Great Lakes Basin Ecosystem. Buffalo, NY: State University of New York; 1989: 109.

Laidlaw J, Allison D, Clarke EA et al: Workshop Report. Reducing deaths from breast cancer in Canada. *Can Med Assoc J* 1989; **141:** 199.

Risch HA, Weiss NS, Clarke EA, Miller AB: Risk factors for spontaneous abortion and its recurrence. *Am J Epidemiol* 1988; **128:** 420.

Walter SD, Clarke EA, Hatcher J, Stitt LW: A comparison of physician and patient reports of Pap smear histories. *J Clin Epidemiol* 1988; **41:** 401.

University of Toronto:

Chan HSL, Canton MD, Gallie BL: Chemosensitivity and multidrug resistance to antineoplastic drugs in retinoblastoma cell lines. *Anticancer Res* 1989; **9:** 469.

Chapman JW, Mobbs BG, Hanna WM, Sawka CS, Pritchard KI, Lickley HL, Trudeau ME, McCready DR: Standardization of biochemical estrogen and progesterone receptor values. *Breast Cancer Res Treat* 1989; **14:** 176.

Dunn JM, Phillips RA, Zhu X, Becker AJ, Gallie BL: Mutations in the RB1 gene and their effects on transcription. *Mol Cell Biol* 1989; **9:** 4594.

Dunn JM, Zhu X, Gallie BL, Phillips RA: Characterization of mutations in the RB1 Gene. *In:* Caveen W, Hastie N, Stanbridge EJ, eds. *Current Communications in Molecular Biology, Recessive Oncogenes and Tumor Suppression.* Cold Spring Harbor, NY: Cold Spring Harbor Laboratory; 1989: 93.

Gallie BL: Rare infant retina tumor reveals cancer basics. *Future Health* 1989; **11:** 7.

Gallie BL: Retinoblastoma. *New Directions In Cancer Treatment* 1989: 612.

Hanna WM, Mobbs BG, Chapman JW, Trudeau ME, McCready DR, Sawka CA, Pritchard KI, Lickley HL: The relationship of ERICA and biochemical ER and PgR with tumour size and nodal status in primary breast cancer. *Breast Cancer Res Treat* 1989; **14:** 165.

Menon IA, Becker MAC, Persad SD, Haberman HF: Quantitative determination of hydrogen peroxide formed during UV-visible irradiation of protoporphyrin, coproporphyrin and uroporphyrin. *Clin Chim Acta* 1989; **186:** 375.

Menon IA, Persad SD, Haberman HF: A comparison of the phototoxicity of protoporphyrin, coproporphyrin and uroporphyrin using a cellular system in vitro. *Clin Biochem* 1989; **22:** 197.

Phillips RA, Jewett MAS, Gallie BL: Growth of human tumors in SCID mice. *In:* Bosma M, Phillips RA, Schuler W, eds. The SCID Mouse: Characterization and Potential Uses. Heidelberg: Springer-Verlag; 1989: 259.

Zhu X, Dunn JM, Goddard AD, Paton KE, Becker A, Phillips RA, Gallie BL: Germline, but not somatic, mutations of the RB1 gene preferentially involve the paternal allele. *Nature* 1989; 340: **312.**